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MYOCLONUS.

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THE history of myoclonus, though somewhat confused, deserves study, for we may thus see how the observation of a particular kind of involuntary movement took shape, with the need of a new term to describe it, and how in the course of time opinions have varied upon the essential features of the symptom and its cause. Friedreich (1881) described as a new disease *paramyoclonus multiplex*, a malady distinguished by abrupt clonic contractions of skeletal muscles. The original case report, of which a summary is presented by Wilson (1940) in his text-book of neurology, attracted wide attention, and the discovery of a new disease was accepted. Ten years later Unverricht (1891) described the clinical picture of paramyoclonus, or, as it has later been named, myoclonus, in greater detail. The contractions, he remarked, resembled those provoked by an induction shock, sometimes affecting single muscles or parts of muscles, though occasionally one might observe a group of muscles in synergic contraction. The contractions often produced little movement of the limbs, but caused widespread, random twitching, resembling that seen in severe febrile illness. When whole muscles or groups of muscles were affected, involuntary movements appeared—flexion, extension, pronation of the arm, abduction or adduction of the shoulders, flexion or extension of the trunk, flexion, extension or rotation in the lower limbs. The contractions were of variable force, extent and distribution, and without rhythm. Both sides of the body might be affected at the same time, but in an asymmetrical, asynchronous fashion.

Some years later, Lundborg (1904) took up the theme, and from his own observations concluded that myoclonus and epilepsy were separate manifestations of a familial disease, of which he recorded several examples. In the first stage of the illness, which began about the age of puberty, there were epileptic attacks, mainly nocturnal. A year or two later myoclonus appeared and, after a time, dysarthria, dysphagia and dementia. Finally there developed widespread muscular rigidity, leading eventually to death after a period of several years. Epilepsy might continue throughout the disease or cease as the myoclonus and other symptoms developed. Thus was founded the concept of myoclonus with epilepsy, the Unverricht-Lundborg disease. The epileptic nature of myoclonus appears not to have been recognized by these or later writers, and it is of interest that Mott in 1907, recording two cases in siblings corresponding in every particular with the Unverricht-Lundborg pattern, entitled his paper "Paramyoclonus with Epilepsy". Yet Russell Reynolds (1861), one of the early physicians at the National Hos-

pital, Queen Square, had given an excellent account of myoclonus as an epileptic variant. He observed the shock-like nature of the muscular contractions and their variable extent and force, noting that they might be so slight that the patient was hardly aware of them, or so forceful as to cause violent jerking of the limbs and even throw the patient to the ground. He also observed that the involuntary contractions might involve the muscles of speech, deglutition and respiration, interfering seriously with these functions and causing the patient to emit strange sounds. Little notice was taken of these observations until Muskens (1928) published his classic work on epilepsy, in which he insisted that myoclonus should be regarded as an essentially epileptic phenomenon, supporting clinical observation with experiment. By injecting monobromide of camphor into cats he was able to produce both myoclonus and epilepsy, and noted that a state of myoclonus might lead to an epileptic attack. This sequence of events is, as Russell Reynolds and Muskens both observed, a common occurrence in epileptics of the so-called idiopathic group, and is especially frequent in the first hour or two after waking. After a period of freedom from seizures the patient begins to have a few random jumps or jerks of the limbs after getting up in the morning. They are most noticeable in the arms, so that, for example, the shaving brush may be flung out of the hand by involuntary movement. The jumps may occur thus for a few mornings in succession without further event. Then there is a morning on which they become more frequent and lead to a generalized major seizure. This is without doubt the commonest variety of myoclonus, but there are many others. *Petit mal* provides an example. In this variety of epilepsy, about which so much has been written in recent years, the onset is usually in childhood and the attacks occur with great frequency, their clinical form having been described by Lennox (1951) and others under three headings—momentary loss of consciousness, single myoclonic seizures, and falling attacks, the so-called *petit mal* triad. From my own observation I am doubtful whether the falling attacks should be considered as a separate form of attack, the fall being probably due to a myoclonic seizure so brief that it is difficult to watch, and so extensive that the patient is thrown to the ground.

In certain cases myoclonus may be a much more prolonged and conspicuous feature of idiopathic epilepsy. Of this myoclonic variant Wohlfart and Hook (1951) have given an excellent account, but I shall refer for illustration of this group to the description given by Dawson (1946) of three cases in which the electroencephalographic changes were also recorded. In an epileptic colony of 450 resident patients he found six who in addition to their fits showed more or less prolonged episodes of myoclonus, which were of two kinds. The commoner variant was that in which the occurrence of a fit was preceded for about two hours by a severe myoclonic status. This is described as follows.

> These patients suffer from jerkings of the muscles which are sufficiently powerful, when they occur in the legs, to cause the subject to fall heavily to the ground; or when they occur in the arms, to cause him, if he is holding some quite heavy object, to throw this over his head. In neither of the patients investigated are the jerks, which are extremely brief, associated with detectable changes in consciousness. Usually the jerks occur at progressively shorter intervals over a period of 1 to 2 hours until one of them passes with little pause into the tonic stage of a major convulsive seizure. Occasionally after becoming more frequent the jerks occur less often and then cease. . . . Any excitement or attempted exertion tends to aggravate the jerkings and may precipitate the terminal seizure.

The other less common variant studied by Dawson was represented by a patient who, besides having major convulsive seizures, was subject to attacks of mild muscular jerkings lasting for a period up to forty-eight hours. Dawson thus describes the attack:

> At the beginning of the attack there is a slight clouding of consciousness and the twitching of the muscles is diffuse and irregular. After about twelve hours the clouding of consciousness disappears and the jerkings become synchronous in all parts of the body and regular at about 3 per second.

Here we have an observation of considerable importance. Most authorities have insisted that for the diagnosis of myoclonus the involuntary contractions must be asynchronous, asymmetrical and arrhythmic. In all these respects the case just quoted was atypical. Should it therefore be excluded from the category of myoclonus? I am sure that it should not, and that although asynergic, asynchronous, asymmetrical and arrhythmic contractions are the rule in myoclonus there are many exceptions, especially when the myoclonus, instead of being occasional, develops into a myoclonic status. To the discussion of the electrical phenomena in Dawson's cases I shall return later.

Myoclonus, either in its occasional form or in bouts of myoclonic status, may also be observed in patients not subject to major seizures or to minor seizures of any other type. However, there is frequently a family history of epilepsy in such cases. I have a youth now under my care who has exhibited myoclonus in both forms since childhood. There has never been any ascertainable disturbance of consciousness or any major seizure. His father and a paternal aunt have epilepsy of the ordinary kind.

All who have carefully observed myoclonus as it has so far been described have commented on the factors which may provoke or aggravate the condition or, on the other hand, relieve it. Of the provoking factors, voluntary movement is the most striking, and it is at the beginning of a movement that the involuntary jerk occurs. This phenomenon has led Wohlfart and Hook (1951) to the statement that the muscle twitchings in myoclonus are typical "action myoclonias", but that this is an overstatement anyone can verify by observation. Myoclonus is often present at rest, though exaggerated by action. It does, however, as a rule disappear during sleep. Pierce Clark (1912), finding an exception to this rule, a patient who stated that he was often woken by a burst of myoclonus, took the trouble to observe him during the night and found that the attacks invariably occurred at the beginning of a movement during sleep. Hodskins and Yakovlev (1930), from close observation of a number of myoclonic patients, concluded that the minimum amount of myoclonus was present when the patient was resting in a completely relaxed, comfortable position—for example, lying in bed. As soon as he was asked to sit up or turn from one side to the other the myoclonus would increase. Observing more closely the influence of change of posture and of voluntary movement on myoclonus, they noted that myoclonic contractions occurred promptly at the beginning of the change of posture—that is, during the moment when the postural shift takes place. They noted also aggravation of myoclonus at the moments of going off to sleep, and of waking, and came to the conclusion that myoclonus should be regarded as a disturbance in the sphere of static and postural neuro-muscular function. Whether the function concerned is phasic or postural, it is at any rate certain that it is at the begining of a movement or a change from one movement to another that myoclonus is exaggerated, whereas continued rhythmic movement may give relief. Some myoclonics find for themselves that they can get ease by walking about.

Related to movement as a provoking factor is muscular stretch. We owe again to Dawson (1947) a series of remarkable observations on this point. The subject was a man, aged forty-two years, with myoclonus as the predominant symptom of what proved to be a progressive encephalopathy, though he also had generalized epileptic seizures. The jerks in this patient, which usually involved both legs, spreadings to the arms, face and diaphragm, were produced by any sudden active or passive movement or by any stimulus to the patient, such as a jar applied to the bed. Examination of the reflexes was complicated by the fact that a tap on a tendon was usually followed by a generalized jerking, whether the stimulus was applied to an arm or leg. Dawson was able to prove that the only sensory stimulus capable of provoking a myoclonic outburst was muscle stretch, and showed further, by means

of simultaneous electroencephalographic and electromyographic records, that the muscular twitch followed the arrival in the sensory cortex of the afferent stimulus at an appropriate interval, allowing the time taken for the impulse to travel up the afferent and down the efferent pathway. This observation suggests that the factor activating myoclonus in movement, whether phasic or postural, may be muscle stretch, and that the absence of such stretch is responsible for the diminution or absence of myoclonus in sleep or relaxation.

Other precipitating factors also are well known, of which the most important for experimental purposes is photic stimulation. It is now generally recognized that in patients having myoclonic seizures myoclonus can often be provoked by a light flickering at a given rate, and especially if associated with eye closure. I have observed one patient with intermittent myoclonic attacks in whom, when he was in a severe phase, the jerking could be precipitated at will by means of an electric torch shone into the eyes, the flicker being obtained by the extended and abducted fingers of the observer's hand moved rapidly to and fro between the source of illumination and the patient's eyes. Of very great interest in this connexion is the observation that myoclonus can be produced in normal subjects by the combined use of flicker and sub-convulsive doses of "Metrazol", an illustration of the truth that we are all potentially epileptic.

Stimulation of the skin and auditory stimuli are also observed to excite the jerks in myoclonic subjects, especially if the stimulus is sudden and unexpected. One patient under my observation would exhibit myoclonus if someone came unexpectedly into his room. Whether in such instances the effect of the stimulus is direct or mediated through its effect upon muscular tension is a question which deserves further inquiry.

There is another distinct variant of myoclonus upon which I have recently recorded some observations under the title of nocturnal myoclonus (Symonds, 1953), which I admit is inaccurate, for the occurrence of myoclonus is related to sleep whether nocturnal or diurnal. In this variety the patient's chief complaint is of insomnia due to the jerks. Just as he is dozing off he is started unto wakefulness by the involuntary jump, and this may recur again and again for several hours. Once sleep is obtained it is usually unbroken, but may be interrupted by myoclonus occurring during sleep. As in the other varieties of myoclonus, the extent and force of the contractions are variable.

Turning now to the abnormalities in the electroencephalogram seen in association with myoclonus, we find all observers in agreement that when any abnormality is found, and this is usual, the essential feature is the appearance of very brief, high-voltage discharges, or spikes. These are not localized in any particular part of the cortex, but are universal and synchronous. In the myoclonic subject single spikes conforming with this description may occur without any muscular contraction, but a succession of spikes is associated with observed myoclonus, and the violence of the muscular contraction is roughly proportional to the number of spikes contained in a volley. The outburst of spikes precedes the muscular contraction, and the muscular contraction as recorded by the electromyogram shows action potentials that have neither more phases nor greater duration than those evoked by eliciting a knee jerk with a tendon tap. It is impossible to produce anything as brief as this by voluntary movements even of the shortest duration. In addition to the spike discharges in the electroencephalogram, and usually following them, there are slow waves at a rate of about three per second. This is the general rule for myoclonus; but in the case recorded by Dawson (1946), in which a myoclonic status of mild degree continued for as long as forty-eight hours, a somewhat different electroencephalographic pattern was observed. During the initial period, in which there was diffuse and irregular twitching in all parts of the body, the electroencephalogram showed a continuous discharge of slow waves and irregular spikes. After five or six hours, when the jerking became regular and synchronous in different parts of the body, the electroencephalographic pattern changed to a regular wave and spike rhythm at a rate of three per second of the type seen in *petit mal*. In this phase, then, whether regarded from the clinical or the electrical viewpoint, the patient may be said to have been in a *petit mal* status of myoclonic type. In the case investigated by Dawson (1947), when myoclonus was evoked by muscle stretch, the electrical discharge in the sensory area was immediately followed by a universal, synchronous and symmetrical spike discharge in the cortex preceding the muscular jerk. A similar electroencephalographic pattern has been observed when a jerk is elicited in the myoclonic subject by photic stimulation, and in the normal subject when myoclonus is provoked by the combination of photic stimulation and "Metrazol" (Gastaut and Roger, 1951). Similar universal, synchronous and symmetrical spike discharge has been observed in association with myoclonus associated with organic cerebral disease. Thus the phenomenon of myoclonus, whatever its setting, seems to be accompanied by a pattern in the electroencephalogram which shows little variation, and the simultaneous appearance of the abnormality all over the cortex suggests a central, subcortical focus of discharge. Penfield and Rasmussen (1950) suggest that all epileptic seizures having this type of electroencephalogram arise from the diencephalon. Jasper and Fortuyn (1947) have produced comparable electroencephalographic records by experimental stimulation of the monkey's thalamus. As the result of these and other electroencephalographic observations there has developed the concept of central epilepsy—that is to say, epilepsy resulting from a central, and possibly a thalamic, discharging lesion, and it would seem probable that myoclonus is one of the clinical expressions of such focal discharge.

We can now begin to regard myoclonus as a special kind of focal epilepsy arising from central structures and, having done so, can proceed to follow the general principle that symptoms depend upon the localization of the lesion rather than its pathology. We shall thus be prepared to find that myoclonus may be a symptom of many diseases. Of this it is not difficult to find examples. The clinical syndrome described by Lundborg of major epilepsy, myoclonus, progressive dementia, dysarthria and rigidity, is one and deserves the title of the Unverricht-Lundborg disease. The disease independently described by Dawson (1934) as inclusion encephalitis and by van Bogaert (1945) as subacute sclerosing leucoencephalitis provides another example.

A few years ago I examined a six year old boy with a recent history of intellectual deterioration followed by the appearance of jerky movements. On examination, he was drowsy and apathetic and presented a continuous series of myoclonic jerks. These were of slight degree, and produced a picture of widespread, random twitching in the limbs, trunk and face, and were associated with widespread synchronous outbursts of spikes in the electroencephalogram. There were no abnormal physical signs. The clinical symptoms, therefore, were those of a myoclonic status, confirmed by the electroencephalogram. In this case investigation of the cerebro-spinal fluid showed a paretic curve without other abnormality—a characteristic feature of inclusion encephalitis; but it was only after two or three weeks that rhythmic torsion spasm developed, with associated runs of slow waves in the electroencephalogram, making the diagnosis certain.

Cerebral lipidosis also may begin in much the same way, and we have to bear in mind that this disease is not confined to childhood.

A man, aged twenty-eight years, under the care of my colleague, Dr. E. A. Carmichael (1953), who was finally proved at post-mortem examination to be suffering from cerebral lipidosis, had been in normal health till the age of thirteen years, when he began to have epileptic seizures, both of the *grand mal* and the minor type. The minor seizures increased in frequency so that by the age of sixteen years he was an invalid. At the age of twenty-one years he developed myoclonus, at first in the lower and then in the upper limbs, the jerking being at times so violent as to throw him out of his chair. From this time onwards myoclonus of increasing persistence and severity was the predominant symptom, together with major epileptic seizures and the development

of dysarthria, nystagmus and signs of pyramidal disease in the later stages. There was no gross mental deterioration, nor any detectable loss of vision, and the fundi were normal, though examination of the retina after death showed typical lipid degeneration of ganglion cells. The cortex was relatively little involved except for the Betz cells, the parts chiefly affected being the medial nucleus of the thalamus, and other parts of the basal ganglia, and the cerebellum.

I mention this case only as an example of the fact that myoclonus may be the outstanding symptom in this disease. I have also met with epilepsy and myoclonus as the initial symptoms in more typical cases beginning in earlier childhood and with a shorter course.

Ramsay Hunt (1921) recorded four cases in which myoclonus and epilepsy were associated with progressive cerebellar ataxia, and a further two cases of twin brothers presenting myoclonus with epilepsy and the signs of Friedreich's ataxia. In one of these cases an autopsy was obtained and showed severe atrophy of the dentate nuclei in addition to the expected changes in the spinal cord. For this group of cases he coined the cumbrous term *dyssynergia cerebellaris myoclonica*; but it seems probable that the syndrome described represented not a new disease, but an unusual extension of the disease process in cases of progressive cerebellar atrophy and Friedreich's disease to involve those structures upon which myoclonus depends. The association with cerebellar disease, however, may be significant, as we shall see when we come to consider questions of morbid anatomy.

Wohlfart and Hook (1951) have recorded three cases of hepato-lenticular degeneration, one with post-mortem proof and the two others both presenting the pathognomonic Kayzer-Fleischer ring, in which widespread and severe myoclonus was the earliest symptom.

There is thus abundant evidence that myoclonus may be a prominent symptom in a number of progressive encephalopathies of different pathological types; but in the great majority of cases myoclonus, like the other epilepsies, is unassociated with any clinical or pathological evidence of organic disease. This is the idiopathic group. The following case is an example.

I was asked to examine a single woman, aged forty-seven years, who had lived for twenty years in a nursing home for patients with functional nervous disorders, with the diagnosis of hysteria. Her symptoms took the form of involuntary movements, difficulty with speech and swallowing, and inability to walk. These symptoms, however, were not continuously present. They might be absent for several months at a time, and would then return for a period of weeks or months. When she was well she was able to live a normal life. This patient when I saw her was in a severe myoclonic status, which as I watched it developed into a generalized tonic epileptic seizure, and there was no doubt from inquiry that she had had at least one previous attack of this kind. Later I had the opportunity of observing her in hospital. At rest myoclonus was minimal, but any active or passive movement would at once provoke it. Speech was unintelligible, mastication and swallowing were severely impeded, and voluntary movement of the limbs interrupted by the jerks to the extent of their being rendered useless. She later died of pneumonia, and Dr. J. G. Greenfield was unable to find any histological evidence of abnormality in her brain.

It would seem that in this case the basis of the disorder must have been a selective and reversible biochemical lesion.

Of the histopathology of myoclonus there is little to be said. In the progressive encephalopathies with myoclonus as a prominent symptom the extent of the damage is so great by the time death occurs that it is well nigh impossible to correlate symptoms with lesions. However, van Bogaert (1950) concludes that when true myoclonus has been present in life, lesions have always been found in the olives, the dentate nuclei, and to a lesser extent the *substantia nigra* and optic thalamus. The involvement of the cerebellum is of particular interest in view of Ramsay Hunt's observations, and of the finding by Greenfield (1953) of an almost complete disappearance of the Purkinje cells in the case reported by Dawson (1947), in which myoclonus was proved to be provoked by muscle stretch. It is possible, as van Bogaert (1950) suggests, that myoclonus may represent a suppression of inhibition, and that the inhibitory circuits involved may utilize cerebellar pathways.

To sum up, I believe we are entitled to regard myoclonus as a species of focal epilepsy arising from discharges in central structures, thus conforming with Jackson's definition of epilepsy as the result of occasional, sudden, excessive, rapid, local discharges in the grey matter. Jackson held to the belief that the origin of the discharge must be local, even though its effects appeared generalized, and in this once again his reasoning has proved right. Myoclonus, therefore, is a symptom of localizing value comparable in this respect with other varieties of focal epilepsy. Its presence does not indicate any special pathology. But as in the case of other localizing symptoms, myoclonus may provide a clue to pathology because of the selective incidence of certain diseases upon particular parts. Diseases such as inclusion encephalitis, lipidosis and hepato-lenticular degeneration, and especially the Unverricht-Lundborg disease, are for this reason apt to cause myoclonus. We have not yet enough evidence from histopathology to indicate what part must be affected to cause myoclonus, though what slight evidence there is suggests that it may be the cerebellum. However, in most cases of myoclonus there is probably no lesion in a histological sense, this being equally true of many other epileptic variants. In such cases we may assume the existence of some highly selective biochemical disorder.

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THE ROLE OF NERVOUS FACTORS IN COLONIC DISORDER.

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. . . his bowels did yearn upon
his brother; and he sought where to weep; . . .
—GENESIS, 43: 30.

THE close relationship between emotional states and the function of the bowels has been known since earliest Old Testament times. Recently this relationship has been more clearly defined and the means by which the changes are mediated better understood.

In a previous communication (Robinson, 1953) it was pointed out that alterations in the function or structure of an organ could be produced by nervous activity that might be due to interference at various levels between the cortex and the periphery; and a mechanism by which certain emotional states might produce peptic ulceration was discussed. The sequences by which such states may affect the colon are less well understood, but it seems reasonable to presume that the general mechanism is the same.

Physiology.

The vagus supplies the caecum and the first part of the colon, and the sacral outflow the remainder of the large bowel. As in the stomach, these parasympathetic impulses cause hyperæmia and engorgement of the mucosa, with increased mucus secretion and contractile activity. Likewise the sympathetics cause an opposite effect. Grace, Wolf and Wolff (1951) state that the gastro-colic reflex in man is not abolished by bilateral vagotomy and that it does not depend on the entry of ileal contents. They presume that it is mediated through the sacral outflow. Groen (1947) quotes from experiments on animals, in which the administration of parasympathetico-mimetic drugs produced spasm of the colon, followed by ischæmia and finally by erosions and bleeding.

In the stomach acute ulcers have been shown occasionally to coincide with cerebral injury. No record has been found of similar occurrences in the colon, but functional alterations may result from stimulation of the hypothalamus or of the frontal cortex. McDonald (1951), reporting the work of Hess, states that stimulation of the hypothalamus in the cat may cause simple defæcation, whereas that of the *septum pellucidum* may result in the complete performance of searching for a site, the appropriate posturing and then defæcation.

> This is because the hypothalamic influence is almost solely on the viscera; whereas more anteriorly somatic movements are co-ordinated with visceral activity.

Stimulation of sympathetic centres in the hypothalamus causes inhibition of intestinal movements (Best and Taylor, 1950). Evidence that cortical stimulation produces changes is less well established; but Arteta (1951) quotes from experiments in which stimulation of Area 6 in monkeys resulted in an increase in intestinal peristalsis, even to the extent of intussusception. Stimulation of Area 8 affects the motility and secretory activity of the gut (Samson Wright, 1952). Frontal lobectomy may lead to fæcal incontinence.

Such physical factors cannot be evoked to explain the ordinary clinical alterations in colonic function. Another origin must be sought for.

Psychological Aspects.

Psychological aspects of altered colonic function and structure have been discussed frequently, particularly in relation to functional diarrhœa and idiopathic ulcerative colitis, as the same personality pattern is commonly seen in patients with both conditions. More recently attention has been paid to constipation and to states in which this alternates with diarrhœa.

Grace, Wolf and Wolff (1951) from their observations on four subjects with colonic fistulæ have added to our knowledge. In two patients with ulcerative colitis increased fragility of the colonic mucosa was observed to occur during periods of resentment. When this was prolonged, petechiæ appeared in one and petechiæ with ulcers in the other. Later, when they were relatively free from serious conflict, their lesions receded. In these cases, emotional conflict could produce both functional and organic disorder. These authors draw attention to the parallel state of affairs observed in the stomach of their subject, Tom, described in an earlier work (Wolf and Wolff, 1943).

The idea that all the emotional changes result from the disease probably arose because ulceration is already established when most patients are studied from this viewpoint. However, when these emotional changes are examined, they are seen to be other than would have been expected should this be the case, and with a more painstaking anamnesis it is frequently possible to show that the basic personality pattern is of much longer standing than the organic component of the disease. Groen (1947), for example, states that in his cases of ulcerative colitis the emotional conflicts were revealed in the histories before the onset of colitis.

Patients with ulcerative colitis are variously described as being neat, ritualistic, and fastidious to the extent of being "old maidish" if a woman, or "old womanish" if a man. They are said to be immature, dependent and insecure; to be lacking in ambition and aggression; egocentric, yet with a hesitant attitude towards their own value; anxious to please and gain approval; and in need of love, yet with an immature conception of its demands.

Many of these characteristics are understood when it is realized that these people's basic attitude is to face difficult situations by being pleasant. They continually pay the insurance of placation by making every effort to keep peace at all times and avoid hostility because they tolerate it poorly in others. It is these traits that make the student wonder how it can be that these charming sufferers are considered the victims of a neurotic illness.

However, this complacent and pleasing exterior is a façade that may hide feelings of anger, resentment and frustration; of indecision, insecurity and anxiety; and of a need for love and support. Grace, Wolf and Wolff (1951) observed that when these emotions were evoked their patients' colons became hyperactive and diarrhœa occurred: they were sweet and angelic, yet hostile; calm and timid, yet rebellious; passive and complacent in behaviour, and yet aggressive within.

The foregoing account explains, to some extent, how patients with chronic diarrhœa may react to the appropriate types of emotional stress, but hardly why they do so in this way. In the patients with the duodenal ulcer the same types of stress—frustration, anger and anxiety—also evoked a parasympathetic response to their feelings of insecurity, but with them, it was in the stomach, while their whole attitude was that of aggression. They strove for security by seeking material gain—clearly a different basic approach.

It has been elsewhere explained (Robinson, 1953) that, in times of stress, the subject tends to fall back to an earlier stage of development, and that in the patient with a peptic ulcer this is to what psychoanalysts call the oral stage. They refer to the next period as the anal stage. This begins soon after the sucking period is over and attention is focused on the bowel function. The infant learns that interest, pleasure and gratification may be derived from the act of defæcation. During toilet training he becomes aware of the value of the stool, which can be given freely or else withheld, and which therefore can be used as a means of playing on the mother's emotions. This concept is often reinforced by the great interest many mothers show in their children's excreta. Later on, the attitude is changed and the fæces become disgusting, so that the adult can use them aggressively as a symbolic soiling weapon.

Prugh (1951), from his studies of 16 children with ulcerative colitis, observed that in all cases there was dominating, rigid, over-indulgent and inconsistent handling

by one parent, usually the mother, which resulted from her own unconscious emotional needs. In nine the domination was most intense during the toilet training. The child's reaction to such pressure was a desire to conform both in bowel habits and in general behaviour, coupled with a wish to rebel in both spheres. Later in life, when the children were expected to achieve independence, they were faced with the same conflict between conformation and rebellion.

A Combined Approach.

The hyperæmic fragile colon must be more susceptible to injury, and normally harmless contents or spasms then possibly may cause ulceration. However, the view has been expressed (Penington, 1948) that the difference between the nervous colon and that with ulcers is more than one of degree. This would be in keeping with the general concept that any pathological lesion must be regarded as being due to the presence of multiple causative factors.

It is known, for example, that lysozyme is present in increased amounts in active ulcerative colitis. Grace, Wolf and Wolff (1951), by applying it to the bowel mucosa, produced local erythema and induration. Its mucolytic action on the protective coating may expose the underlying membrane to the action of the indigenous bacteria or to other traumata. Their quoted data relating to amœbic infestation are also significant. In the temperate zones of the United States of America 5% to 10% of adults are carriers, yet cases of acute dysentery are rare. Some exacerbations were shown to have occurred in situations of stress, conflict and anxiety. This picture is further complicated by the suggestion (Annotation, 1953) that the favourable effect of antibiotics in this disease is due to their action on the symbiotic bacteria rather than directly on the amœbæ themselves.

Following on this lead, I examined my records of patients with achlorhydria, having in mind that diarrhœa is by no means an invariable complication of this condition—it is relatively rare, for example, in patients with pernicious anæmia—and that when present it is notably intermittent.

Of 31 patients with achlorhydria, 11 suffered from attacks of diarrhœa of sufficient frequency to have been recorded. Unfortunately, many of these patients were examined before the possible association of a specific personality pattern had been considered, but all had other stigmata of neurotic illness. In all but one it had been noted that the attacks were related to emotional upsets, and in retrospect five had the typical personality described. Hydrochloric acid had been given to five; only one claimed any benefit.

By way of comparison 12 of the 31 patients suffered from flatulent dyspepsia. Ten were given hydrochloric acid, and all of these were helped by it, although eight had other nervous symptoms. Six of the 31 patients suffered from constipation. Five of these had associated nervous symptoms of a depressive type.

The following is an illustrative case.

Mrs. X. first developed bouts of diarrhœa in 1933 when aged forty-seven years. These usually lasted for two to three days, after which she became "constipated". She then took an aperient and the cycle recommenced. The motions contained mucus but not blood. When I first examined her in 1947 she was found to have pernicious anæmia with its associated achlorhydria. The anæmia responded to liver therapy, but the diarrhœa continued despite the use of hydrochloric acid.

Her personality was of the type described. She was pleasing, tidy and unaggressive, and she refused to admit to any source of worry or to the knowledge of any cause for the diarrhœa. However, her dreams were symbolic of frustration. Her son stated that the attacks always occurred when her set, rather restricted pattern of activity was disturbed, as when guests were anticipated, or more particularly, when she visited their seaside week-end cottage. It was later learned that these seaside visits had been uneventful until new neighbours arrived, who proved to be old enemies.

In this case, as in many others in which chronic diarrhœa was a feature, it was observed that attacks of the common infective enteritis lasted far longer than would be expected if these cases were compared with other cases in the same epidemic.

It would seem, therefore, that in some cases of chronic diarrhœa other factors must be present coincidently with the nervous factor to initiate or perpetuate an attack. Whether this is so in ulcerative colitis is unknown in the present state of our knowledge. Alexander (1952) makes the following statement:

> Some specific local somatic factor may be responsible for the fact that in some patients anal regression produces ulceration in the bowels. It is quite probable that the specific factors will turn out to be not psychological, but the peculiarity of the physiological mechanisms initiated by the emotional stimuli. . . . It is important to consider the fact that the same type of conflict situation is found in compulsion neurotics and patients suffering from paranoid symptoms who may not have any significant bowel disturbance or any somatic symptoms.

It would be of value if all cases of diarrhœa of whatever cause were examined with this in view. The presence of a neurosis or of a few diverticula, for example, should not blind one to the possibility that either may be merely contributory.

Discussion.

The foregoing brief review may be used as a basis for explaining the typical personality earlier described in patients with chronic diarrhœa.

The feelings of guilt associated with the suppressed rebelliousness cause this to be over-compensated to produce the sweet, angelic façade; while those associated with the disgust could be responsible for the cleanliness and neatness; and both for the patients' reticence in discussing their emotions. Their characteristic lack of insight regarding the emotional factors of their disease, which seems so odd when their reasonably high intelligence level is considered, is probably a protective blocking. The obsessional, perfectionist and ritualistic traits spring from their rigid training. Their dependency and intolerance for hostility which arise in their desire to conform, make it difficult for them to satisfy their aspirations and add to their frustration; while their ambivalent feelings of resentment and love towards the mother or her substitute seem to threaten them with loss of their main source of support and thus add to the anxiety resulting from the other conflicts. Their regression to the infantile state is well illustrated by the need for attention which the condition demands, the messiness, the diapers and the occasional incontinence.

The foregoing mechanisms are unconscious ones, and so the patient can maintain the pleasing calm façade and may honestly deny that he has any worries.

From the foregoing account, the patients' morbid interest in their bowel function and stools is easy to understand, though the reason for their lack of self-consciousness and indeed eagerness in discussing these matters is not so obvious. Perhaps this is, as Larkin (1943) suggests, because they "have, as it were, lived among strangers all their lives and have never been sure that their feelings are understood. Therefore when they do get the ear of a doctor, a lifetime of repressed feeling becomes released to the first person who is prepared to meet them on the rectal level".

This account now enables us to understand the psychological basis for constipation, for if "taking in" is the characteristic of the peptic ulcer patient who seeks security by aggressive acquisitiveness, and "giving out" that of the patient with chronic diarrhœa who seeks his security by paying "danegeld", then "holding on" to his one talent is the method adopted by the constipated man.

Constipation is common in patients with depressive psychoses and in those with persecutory delusions. Alexander (1952) states that chronically constipated patients have a trace of both attitudes—the distrust of

paranoia and the pessimism and defeatism of melancholia, a typical emotional undertone being, "I cannot expect anything from anybody, and therefore I do not need to give anything, I must hold on to what I have". Grace, Wolf and Wolff (1951) regard the predominant emotion as that of depression. A typical situation was that of one "grimly determined to hang on to his allotted task, even where he saw no special advantage or hope of respite". They describe the characteristic combinations of being tired and tense, listless and restless, alert and depressed, struggling yet discouraged, seeking relaxation yet not capable of experiencing it and of craving sleep yet sleeping poorly.

They further usefully group together the conditions known as mucous colitis, spastic colon and irritable colon as the syndrome of alternating constipation and diarrhœa, and show that, in their cases, these symptoms were present in association with the appropriate mood. In the diarrhœal stages the colon was such as is seen during parasympathetic activity and in constipated phases, as following sympathetic stimulation—namely elongated, dilated, hypotonic and with decreased secretions. Cannon observed general gastro-intestinal hypomobility—that is, sympathetic effects—during pain and fright; but the former authors point out that this is the uncomplicated reaction, and that the colitis pattern was evoked if the pain was associated with resentment or chronic anxiety. This may be compared with the observation quoted elsewhere (Robinson, 1953) that chronic fear may produce parasympathetic effects, while acute fear leads to sympathetic ones.

Treatment.

When one is called on to help a patient with chronic diarrhœa, whether with or without ulceration, the ordinary measures involving rest, antispasmodics, sedatives, adsorbents and diet must be employed; but it must be realized by the physician, and through him by the patient, that these are merely supportive measures. Full and permanent relief will be found only when the emotional problems are adjusted.

From what has been said, there seems no object in employing this supportive therapy during remissions, and especially so after the patient has gained some insight into the cause of his disease. I advise my patients to return to it when they feel that they cannot cope with a situation such as might previously have precipitated an attack. They must be warned against the use of drastic aperients, for such is the anxiety regarding bowel function that a smart purgative is almost invariably taken after the two or three days of "constipation" that follow a bout. I have never seen any benefit follow the use of sulphonamides or antibiotics that could not be explained otherwise.

The key to finding the precipitating cause is to realize that the approval, support and love they seek is that of the mother or of her substitute, who may be, for example, the husband or wife, the daughter or the doctor himself. The father as a rule is of less importance, unless he threatens to come between the patient and the mother. Attacks may occur when this support is withdrawn in fact or in threat. It must be emphasized that the incident may appear to be quite a minor affair, but one which, none the less, symbolizes rejection by the mother.

How far all this is gone into will depend on the degree of incapacitation and the insight of the patient. Most patients will admit that they get the attacks if upset, many eventually will understand that insecurity is involved, and a few will be able to relate this to the mother as one did when she said, "I have never been the same since mother passed away".

This was Mrs. Y., who in 1940, when aged thirty-nine years, developed congestive cardiac failure with fibrillation when her father died of a myocardial infarct. She had no strong emotional ties to him, but had never been really well since her mother died three years earlier. She was a spoilt, youngest child, nervous and with a tendency to "fainting turns". After marriage she continued to depend on her mother, spending at least three days a week with her. Her father and daughter are now the chief supports in her life as a cardiac invalid.

It is possible to suspect that in part, at least, her cardiac failure has been a visceral equivalent of her anxiety, for it was frequently observed that, even if she was desperately ill, she would recover with amazing rapidity when placed in her favourite hospital, and that she would always discharge her œdema in time to go for a planned holiday. She was examined and investigated by several cardiologists, who were unable to explain her condition.

Early in 1952 she began to have attacks of diarrhœa that was later bloody. At first it was thought that these followed mersalyl injections; then it was realized that the first one also coincided with her housekeeper's attack of *herpes zoster*. The patient obviously resented this, although she would not admit it. In later attacks it was almost always possible to find an emotional cause, and they became particularly severe when her daughter obtained a travelling scholarship.

She wears a diaper even when she has no diarrhœa; but despite this has soiled the bed on many occasions. When at home she lives virtually on oysters and chicken; yet when she is placed in hospital the attacks subside within a couple of days, and within a week she can eat a full diet.

She is, at first sight, a bright, complacent, superficial woman; but she is one who none the less controls the home from the sick-bed with all the terrible strength of the weak. She has had no physical relations with her husband for many years, but he shares her bed and is as tied to her as she is to him. She is anxious and frets when he is away, yet is readily reassured by gifts when he returns. When the daughter went overseas he retired from business.

It may be significant that since the diarrhœa has been present her œdema is very much less than can be accounted for by the dehydration. Fibrillation is still present, but she needs no mersalyl, though she previously required this once or twice a week.

Although she has recently gained some insight the prognosis is poor because of her immaturity, her great dependency, her husband's attitude and the bountiful secondary gains that would be lost should she recover from either of her illnesses.

Patience, tolerance and caution are necessary in treatment, as too precipitate a probing or a ruthless disclosure of what to the physician may seem obvious will cause avoidable and unnecessary distress, and perhaps relapse, or failure to continue treatment. The argument that one has not the time to spend on long sessions with such patients is hardly effective when this is compared with the time spent in and out of hospital with orthodox medical or surgical treatments.

Ideally, treatment along psychotherapeutic lines should be begun early in the course of the disease, because at that time the patient is usually young and facing adult responsibilities for the first time, receptive and with labile behaviour patterns. In this way the process may be arrested before chronic incapacity ensues or complications render surgery necessary. It must be remembered that surgery, besides burdening the patient with a bag "that does not smell if properly cared for", leaves him with his neurosis intact. He is not able to face life more adequately, and his superficial reason for not doing so has been removed only in part.

The aim of treatment is to assist the patient to discover the types of emotional disturbance that bring on the attacks, to assist him to find a means of coping with them, and to teach him to understand their significance—that is, to bring the unconscious mechanisms, which need not be very deeply buried, to the surface. As a rule this is best done by non-directive psychotherapy such as that described by Carl Rogers (1942). This is a method whereby the patient is encouraged to discuss his problems, and particularly his feelings regarding them, with a minimum of interference from the physician. This method was employed with success in the case of a young unmarried farmer.

Mr. A., aged twenty years, was first examined on January 17, 1952. He had had attacks of diarrhœa since 1949 and had passed blood on occasions since 1950. He had been "nervy" since the age of four years, and now had headaches and slept poorly.

At the first interview he was able to relate his attacks to emotional upsets. Thus the onset of the illness coincided with domestic discord at home, and the last attack, which began in July, 1951, followed his rejection from the Navy.

His father and mother had disagreed for years and had been separated for a time ten years before. He said his father was unpredictable—kind one day, bad-tempered the next; but "mother is lovely". She is a sensible, capable-looking woman. She brought him on his first visit. One was reminded of a large yacht with a dinghy in tow. For all his dependency he was able to present a good face by reason of his well-groomed appearance and his attractive eagerness.

After the first visit he was examined each week for periods varying from one-quarter to three-quarters of an hour. At first the main subject discussed was his disappointment on his failure to enter the Navy, which was to have allowed him to leave home. He soon realized that the real reason that he wanted to join this service was because he believed that he could have gained more rapid promotion than his father did when he was a sailor, and would thus have been able to demonstrate his superiority. With this clarified he was able to express a great deal of resentment towards his father, and his health began to improve rapidly. He became much less shy and formed a friendship with a young woman with the same complaint. By March he was able to compare critically her attitude towards her illness with his own in the light of his newly found insight. In April he began constructively planning for the future and found that he could accept criticism from others without resentment, so that by the end of the month he was able to leave for home, confident for the future and with no fears that he would not be able to cope with his father, whose attitude he had, partly at least, come to understand.

He was not examined again until he returned over a year later. Soon after returning home he had had one relapse, which followed an argument with his father, and was aggravated, he said, by the gloomy prognosis his local doctor gave. On recovery, with confidence restored, he undertook a number of contracts painting buildings, and was so successful that he decided to get married. His fiancée's parents refused permission, as they did not consider her old enough. She became pregnant, and he implied that he had been intentionally careless so that he could force the issue. She broke off the engagement; he became drunk and ate pickles without any ill effect. However, he lacked the courage to tell his mother of his dilemma, and that indeed was the purpose of this visit to me. As she again accompanied him on this occasion, this presented little difficulty. He is now married.

The task is frequently difficult, as these patients will make little attempt to change their emotional or environmental *status quo*, preferring, as it were, the devil they know (and depend on) to the one they do not. Some are so inadequate or so lacking in insight that the change must be made for them, as occurs when they are placed in hospital or in a rehabilitation centre. Sometimes other circumstances force a decision, as in the case of an attractive young saleswoman.

Miss B. was aged twenty-one years when her ulcerative colitis commenced in 1947, a week before her proposed marriage. Her doctor told her that she would not be cured for two years. The diarrhœa cleared up in two months; but, although expressing the utmost desire for marriage, she avoided all thought about its physical basis, and her doctor's prognosis satisfied her as a reason for deferring this decision. Her fiancé left her, and she remained well and returned to employment in February, 1952. She was described as an excellent worker, reliable, cooperative, achieving a high standard, intelligent, helpful, popular and sociable.

She became engaged to another man, and her colitis recurred, compelling her to leave work on December 1, 1952. She believed that the breakdown was due to "the pre-Christmas rush at work". Treatment along the lines described was begun on April 28, 1953. She became able to relate her illness to her fears of marriage from the physical point of view, but more to anxiety regarding the loss of the support of her mother and sisters. She eventually decided to marry in November, but became pregnant and was married some months earlier without any recurrence of the colitis. She said: "I walked down the aisle with only half a grain of phenobarb." She had a miscarriage which was not induced, and now is pregnant again and well.

In this case the decision was forced by the pregnancy; but it is reasonable to suppose that without treatment she would not have been able to cope so successfully with this dilemma, and perhaps indeed would not have found herself in it.

The treatment of constipation that does not yield to simple instruction regarding regular habits should be along similar lines, the attack now being directed towards the difficulties that derive from the personality pattern that is seen in this group of patients.

Conclusions.

Any pathological change should be envisaged as representing the resultant of the action of many forces, rather than as being due to one alone. This principle is well illustrated when the role of nervous factors in colonic disorder is considered.

Autonomic impulses, the result of stimulation at peripheral, subcortical or cortical levels, can affect the whole alimentary canal and in the colon may contribute to functional or organic disorder.

Certain personality types are described as occurring in patients with chronic diarrhœa and in those with constipation, and typical conflict situations may precipitate attacks, presumably by way of autonomic mechanisms.

It is not yet possible to state whether the difference between chronic diarrhœa with ulceration and that without ulceration is one of kind or of degree. In both types the psychological background appears to be the same, and in both other factors are probably involved. In some cases the nervous factors seem predominant; but diarrhœa from organic causes may be exploited by neurotic patients and perpetuated to serve their needs. In the treatment of diarrhœa the whole patient must be studied.

In all cases of chronic non-specific diarrhœa orthodox medical or surgical measures should be regarded as supportive, and treatment should include psychotherapy. This may be helpful, too, when another cause is known. Constipation that does not yield to simple instruction should also be treated as a psychosomatic disorder.

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THE MAINTENANCE, STANDARDIZATION AND USE OF PHOTOELECTRIC COLORIMETERS.

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PHOTOELECTRIC COLORIMETERS are being used increasingly for clinical biochemical determinations in Australia. Unfortunately, there is no adequate text-book dealing with the operation of these instruments. While many books on colorimetry discuss the mathematical deduction of the laws of light absorption and give much theoretical physical information on the design and construction of photoelectric devices of various kinds, very few practical operational details are readily available for the chemist. The instruc-

tions issued by the manufacturers in this regard are quite inadequate.

These notes are offered in an attempt to remedy this deficiency to some extent and outline some of the many traps encountered in operating and testing instruments in these laboratories over the past five years. While the notes are written specifically to cover simple single-cell instruments, many of the observations made are applicable to more complicated types. No attempt has been made to cover theoretical aspects, which are adequately discussed elsewhere. (See Bibliography [1] [2] [3].)

The commercial photoelectric colorimeters most widely used at present in Australian clinical laboratories are the E.E.L. photoelectric colorimeter, the Hilger "Biochem" absorptiometer and the Unicam G.P. photoelectric colorimeter. The Unicam D.G. spectrophotometer really belongs to the class also (on account of the wide band width used), and the C.S.I.R.O.-Finlayson hæmoglobinometer, although designed for estimating one substance only, is of the same general design as the others.

COMPONENTS.

These instruments have the following components in common: power supply, lamp, light filters, absorption cells for liquids, diaphragm, a single selenium photo-cell and a meter to measure the photo-cell output. These components will be considered in turn.

Power Supply.

A stable voltage source is most essential, as a 1% change in voltage may result in a 4% error in photometry. The supply may be a battery or a constant voltage transformer.

Transformer.

Batteries, properly cared for, give the more stable output, but for most purposes the transformer is far more convenient and quite permissible—provided it is a constant voltage transformer. Some early ones, apparently supplied in good faith as such, were not. The input voltage to the transformer should lie within the limits specified by the maker, and the frequency of the supply should be very close to that marked on the name plate. This question of stable frequency is often overlooked and is important, since the output voltage variation is about 1·4% for a 1% frequency change.

An unsteady galvanometer needle is more often than not due to a fluctuating voltage supply due either to variation in the source or to bad connexions in the lamp circuit. A transformer which will not hold the galvanometer needle or spot steady is useless. Transformers made by Advance Components Limited, London, have been found very suitable. On no account must these transformers be connected to a direct current source or left on without being connected to the lamp.

Battery.

Two types of battery supply are permissible. A battery of the correct voltage and of large capacity may be permanently sited near the instrument, together with a trickle charger which is switched on as often as necessary during periods in which the instrument is not being used (preferably overnight) to keep the battery on charge. It does not matter if the trickle charger is left on a little longer than is necessary to bring the battery to full charge; it will simply mean that some water will be removed from the cells and, of course, some power wasted. It must be remembered that immediately after charging, the voltage is higher than normal. After charging, a battery should be left for about half an hour to "de-gas", and the lamp of the colorimeter should then be switched on for about ten minutes, after which time the voltage should have dropped to normal. Subsequently, when it is operating, it is necessary only to allow the lamp to warm up for about three or four minutes before use. The colorimeter should never be used with the charger connected. It is convenient to have two switches, one in the mains supply circuit and the other in the charger-battery circuit. This latter switch saves disturbing the contacts at the battery and is necessary, since, if the circuit were left closed, there would be a small back-flow of current through the charger's copper oxide rectifier.

A less desirable arrangement is to have two batteries (preferably radio type) of smaller capacity, one connected to the colorimeter and the other kept on charge within easy access. The batteries should be changed over once a week so as to keep both well charged. System 2 may be converted to system 1 at any time by connecting both batteries in parallel and installing the trickle charger. A battery should never be allowed to remain flat for long or it will be permanently damaged. It must be remembered also that a charged battery will slowly discharge itself in six to eight weeks even if not being used. Should a battery not be required for a period of more than a month, arrangements should be made to have it connected to a charger regularly.

The tops of batteries should be cleaned as necessary by washing the space between the terminals with tap water to remove dust or splashed acid. The terminals, which should be of the brass screw and brass butterfly nut type, should be cleaned at least once a month, any corrosion removed with sandpaper, the terminals smeared with a little petroleum jelly, and the connexions replaced and kept tight. Often the colorimeter is blamed for erratic results really caused by bad connexions at the battery, though sometimes loose lamps, faulty switches and other connexions in the battery circuit may be at fault.

Defects in the battery circuit may be readily detected by the simple expedient of connecting a suitable inexpensive voltmeter in parallel with the lamp and mounting it in a permanent position near the colorimeter. High resistance at connexions or lack of sufficient charge in the battery are then obvious at once.

Batteries should last about three years if well cared for. The condition of the charge in the battery can be readily ascertained at any time by taking specific gravity readings on each cell with an inexpensive battery hydrometer syringe. Specific gravity readings may differ slightly with the make of battery, and the supplier should be asked for figures applicable to the battery in use. The figures given in Table I for one make of battery indicate the readings to be expected.

TABLE I.

Expected Specific Gravity Readings for One Type of Battery.

Condition of Charge in Battery.	Queensland, Northern Territory.	New South Wales, Victoria, South Australia, Western Australia, Tasmania.
Fully charged	1·220	1·250
Half charged or half discharged	1·150	1·180
Fully discharged	1·090	1·120

It is obvious that specific gravity readings are useless if taken immediately after distilled water has been added to the cells. Sufficient time should be allowed for the rising bubbles of gas generated on the plates to bring about the mixing of the contents of the cell. The specific gravity normally should be kept above 1·200 and the plates covered with electrolyte, which should not be more than about a quarter of an inch above the top of the plates. The best time to add water is just before recharge. The level should never be inspected with a naked light, since hydrogen and oxygen are generated at the plates and an explosion may occur.

It is a good plan to find out well in advance where a suitable battery can be obtained on loan, in case the use of the colorimeter is required urgently and the battery is found to be flat. This battery condition should never occur without warning, particularly if a voltmeter is installed in the circuit.

A log book should be kept and details of battery maintenance entered.

The Lamp.

The spectral range and intensity of the lamp depend upon the temperature of the filament and the cleanliness of the glass envelope. The temperature of the filament depends upon the current passing through it, which in turn depends upon the voltage across the lamp, and this may be kept uniform by adhering to the instructions given under the heading "Power Supply". It also depends on the rate of heat dissipation; and if this is not uniform, as often happens if the instrument is sited in a draughty position or not sufficiently warmed up before use, fluctuation in light output will occur. If the instrument is provided with a lamphouse (for example, the Hilger "Biochem"), this should be quite rigid, as a knock during operation may alter the relative positions of filament and exit slit. Lamps have only a limited life, and it is advisable to keep a number of spares. Sometimes, before the filament actually burns out, the output becomes unstable, and the lamp should then be replaced. Replacement of lamps is a very simple procedure (consult maker's instructions).

The Filters.

The filters may be of glass construction (Chance), grating (Unicam spectrophotometer) or glass and coloured gelatin film (Ilford). Of these, the all-glass filters are the most permanent, although the grating is most convenient. Gelatin filters have excellent transmission peaks but are particularly liable to change, especially in the tropics, but also in the temperate zone, owing to fading and to mould and fungus growth. Filters should be stored in a dark, dry place when not in use. In the tropics (and even in temperate climates) it may be necessary to keep gelatin filters in a desiccator in the dark to ensure stability. Gelatin filters should be inspected regularly for signs of such growth, which may start as tiny spots on the gelatin and finish as radiating clusters which cover the whole film. The alignment of the grating in the Unicam instrument should be regularly checked by means of the didymium filter provided, and adjusted if necessary.

The filter should be mounted with its face fixed perpendicular to the light beam. In some of the older "Biochem" instruments the filter may fall over through an angle of approximately 10° in spite of the "Bakelite" spacer—provided, apparently, to prevent this. A small square of black rubber, a quarter of an inch by a quarter of an inch by one and a half inches, placed between the top of the filter and the spacer will keep the filter in position and prevent appreciable errors due to this movement.

The Absorption Cells (or Cuvettes).

The absorption cells (or cuvettes) may be either of fused-glass parallel-sided construction or of specially selected test tubes of various sizes. They must be kept scrupulously clean to give correct results. After use, particularly if alkaline solutions have been used (such as the alkaline copper solutions in blood sugar determinations), they should be well rinsed, first with tap water and finally with distilled water, and inverted in a dust-free position to drain, preferably on a non-fluffy absorbent material to hasten drying.

Before insertion in the holder, the outside of the cells should be wiped with a clean, dry cloth and their contents inspected for turbidity and air bubbles, both of which will make accurate work impossible. They should then be inserted in the correct position in the cell holder of the instrument, without the fingers touching the surfaces which transmit the light beam. Should a solution be spilt on these surfaces they should be cleaned immediately. Cells should be carefully matched and, in the case of test tubes, should be marked to ensure correct alignment in the holder. Surprisingly large variations may be encountered in so-called "matched" test tubes. Often it is possible really to match only a small percentage in a "set of matched tubes". Matching should be carried out first with distilled water for comparison at zero density and then with a suitable density standard solution (see later) for comparison in the middle of the scale. Most workers check the zero position only, whereas the other is equally important. Values should agree to within, at least, 1% for work requiring this degree of accuracy.

Cells should be periodically cleaned with a 1% solution of a detergent such as "Teepol" or "Comprox", or with soapy water, never with an abrasive powder. Occasionally with very dirty cells it may be necessary to use chromic acid. Once cells become cloudy, or optical surfaces chipped or excessively scratched, they should be replaced. Except in those rare cases in which it is stated in the operating instructions supplied with the instrument, it is necessary to determine the minimum volume of liquid required for each cell. It may be determined as follows:

The instrument is adjusted to zero density with the cell filled with distilled water and one of the filters in position. The cell is emptied and placed in the cell holder. A standard solution to match the filter (see later) is run down the sides of the cell from a burette, a fraction of a millilitre at a time, until a constant reading is obtained on the meter. (This will not be the maximum reading, which is obtained when the meniscus is in the light beam.) The burette is then read. It may be necessary to repeat the test a few times to determine the minimum value. In both the Unicam instruments, on account of the type of diaphragm used, it may be found that the minimum volume required depends on the colour of the solution. Unfortunately, most of the cells require volumes which are odd volumes to the chemist: for example, the E.E.L. standard five-eighths-inch tube requires seven millilitres; the hæmoglobinometer requires eight millilitres; the half-inch Unicam tube requires four millilitres; the "Biochem" one-centimetre cell requires six millilitres, and the two-centimetre cell 12 millilitres, *et cetera*. An instrument designed to work with five millilitres and ten millilitres of liquid would suit the chemist's volumetric tools far better, and at the same time allow more accurate photometric readings to be made on solutions of low colour density.

The Photo-Cells.

In these instruments, photo-cells are all of the selenium "barrier-layer" type, and their life is not indefinite. At least one spare should be carried always. The life of the photo-cell may be prolonged by illuminating it only when taking a reading and by keeping the instrument away from strong light, heat and acid fumes. If possible it should be set up in a room other than the one in which the chemical procedures are carried out and in the coolest, dullest position obtainable. Stray light can alter the zero; for example, when the test tube holder is used with the original "Biochem", the large lens on the photo-cell housing is only partly covered and may pick up external light. A piece of quarter-inch black rubber sheet may be easily cut to fit as a light shield.

Sometimes trouble is experienced with the spring contacts to the photo-cell and is evidenced by rapid galvanometer fluctuations despite an apparently steady light source. In this case, the photo-cell should be removed, the contacts cleaned with emery paper and tightened if necessary, and the photo-cell replaced. If this does not correct the fault, other contacts in the photo-cell circuit should be inspected and tightened. Chemicals readily attack the cell surface, and care should be taken that solutions are not spilt anywhere near the photo-cell. Only in the "Biochem" instrument is the cell in a sealed chamber; in the E.E.L. it is possible to spill liquid down the cell-holder opening on to the face of the photo-cell itself. Mr. N. Henry, of the Pathology Department, Brisbane General Hospital, advises that this can be prevented by sealing a large cover glass between the mount and the frame contacts of the photo-cell. The replacement of photo-cells in all these instruments is a very simple matter, and the supplier of the instrument should be requested to furnish details of the procedure and, if possible, arrange a demonstration. This will save having the instrument out of action for excessively long periods. The photo-cell circuit should not be disturbed, however, until the battery circuit has been fully examined.

The photo-cells should never be exposed to strong light, as it rapidly fatigues them, renders their output non-linear and shortens their life. A filter must be always in position

when the instrument is turned on. While the lamp is warming up, light should be prevented from reaching the photo-cell either by using the shutter on the lamphouse ("Biochem") or by placing a black "cell" in the cell holder. When this is not supplied, it can be made from a test tube coated inside with black paint.

The Diaphragm.

The diaphragm regulates the amount of light reaching the photo-cell and normally gives little trouble, though sometimes the one in the E.E.L. instrument shows a tendency to stick. In this case a little petroleum jelly on the moving parts should correct the fault. Care should be taken not to jar the instrument and so move the diaphragm, especially during removal or insertion of absorption cells. In the C.S.I.R.O.-Finlayson hæmoglobinometer there is no diaphragm, the amount of light reaching the absorption cell being constant.

The Meter.

It is most important that the instrument be placed on a firm level bench, especially with both Unicam instruments, which have projected scale meters. Care should be taken to prevent leaning on the two instruments of this make when a reading is being taken, as a slight tilt will move the zero quite considerably. A shaky bench will cause wide meanderings of the light spot. If an instrument is moved, particularly if shipped for overhaul or repair, it is most important to short the meter by putting the switch in the "off" position or, in the case of the "Biochem", by joining the terminals at the rear of the meter with a piece of thick copper wire.

The "Biochem" and Unicam instruments have two scales, a logarithmic density scale graduated from ∞ to 0, and an evenly divided transmission scale from 0 to 100%. This latter scale is of little use in chemical determinations unless the results are plotted on semilogarithmic graph paper. It is far more convenient to use the density scale, the readings on which generally vary in a linear fashion with the concentration of light-absorbing substance in solution. Thus if a 1% solution of a particular substance in a one-centimetre cell gives a density reading of, say, 0·13, a 2% solution should give a value 0·26 in a one-centimetre cell, 0·52 in a two-centimetre cell and 0·13 in a half-centimetre cell. Such relationships permit the use of ordinary graph paper for plotting the calibration curve. These figures will be exact, however, only if the solution obeys Beer's law and the correct filter is used.

In the E.E.L. instrument the density scale has been multiplied by 100 to give whole numbers; thus 0·1 becomes 10, and the scale reads from left to right, in the opposite direction to the other instruments. This 0–100 scale must not be confused with the 0–100% transmission scale of other makes.

Calibration curves may be plotted on ordinary linear graph paper, or in the case in which a standard and an unknown are being compared the calculation simply becomes:

$$\text{Concentration of unknown} = \frac{\text{Density reading unknown}}{\text{Density reading standard}} \times \text{Concentration of standard}$$

Transmission readings can never be used in this manner.

It is to be noted that this ratio $\frac{\text{Reading unknown}}{\text{Reading standard}}$ is the inverse of the ratio $\frac{\text{Reading standard}}{\text{Reading unknown}}$ used with the visual comparitor of the Duboscq type.

The zero of the meter (no light) should be checked occasionally and, if necessary, corrected. This is most important in the case of the Unicam instruments, in which the zero position depends upon the level. It is wise to carry a spare bulb for the projection lamps of the meters of these instruments.

TECHNIQUE.

Choice of Absorption Cell and Dilutions.

It can be shown, on purely theoretical grounds, that the minimum error in photometry occurs when the density reading is 0·4343. It can also be shown that, no matter how accurately the instrument has been constructed, the relative photometric error increases very sharply outside the range 0·15 to 0·7 density. When possible, therefore, a dilution should be chosen to match the absorption cell used so as to bring the reading between those limits. An alternative is to use a larger or smaller absorption cell; but, unless this is of parallel-sided construction, a calibration curve will have to be prepared for each size of cell used. Changing the size of cylindrical cells may considerably alter the optics of the instrument.

When it is found that the density value is higher than 0·7, the solution (and the blank) may sometimes be quantitatively diluted to bring the reading within the range, but it is better to start with a smaller quantity of original specimen.

An example of this would be encountered in the determination of blood sugar levels. If the instrument is calibrated to suit the determination of normal blood sugar levels, it will be found that during performance of investigations on diabetics or in the plotting of a glucose tolerance curve, higher values, outside the range, will be encountered. Using half a millilitre (instead of one millilitre) of diluted deproteinized blood *plus* half a millilitre of distilled water will bring the values within the desired limits.

On the other hand, some determinations, for example, normal serum bilirubin values, owing to the small amount of reacting substance present, will give values below 0·15. In these cases, while little can be done to correct the relative photometric error, errors due to other causes, such as differences in the absorption cells and their positioning, need to be specially watched for and eliminated.

It is always a good plan to read every solution twice thus: (i) adjust zero with blank, (ii) read unknown, (iii) read blank again and adjust again, if necessary, (iv) read unknown again. This will take into account slight changes due to voltage variations, absorption cell positioning and photo-cell fatigue.

Photometric Standardization of Instrument.

Since it has been already pointed out that there are quite a number of factors which influence the results obtained, it is desirable to institute some check to detect alterations in the components when they occur and prevent incorrect results being reported. In the C.S.I.R.O.-Finlayson instrument this problem is partly overcome by the use of a neutral glass filter for testing. Probably the best method of checking all components is with standard solutions of previously determined optical density. Two such solutions are as follows:

(i) Copper sulphate A.R. ($CuSO_4.5H_2O$), 40·00 grammes
(Use analytical balance)
Sulphuric acid 10%, 100 millilitres.
(Use graduated cylinder)
Distilled water to 1 litre
(Use volumetric flask)

(ii) Cobalt sulphate A.R. ($CoSO_4.7H_2O$), 40·00 grammes
(Use analytical balance)
Sulphuric acid 10%, 100 millilitres.
(Use graduated cylinder)
Distilled water to 1 litre
(Use volumetric flask)

The solutions should not be filtered but should be allowed to stand in a stoppered bottle overnight, decanted from any sediment and stored in a dark cupboard in bottles of resistance glass (with glass stoppers coated with petroleum jelly to prevent creep and evaporation) and used periodically to check the performance. Solution Number 1 can be used to check with red and orange, Number 2 with green and blue filters. Thus the analyst has available a ready means of checking the constancy of results being obtained over a period of time and of detecting slow changes due to aging of lamps, filters, absorption cells and photo-cells. The

standard copper and cobalt sulphate solutions will remain unchanged in optical density indefinitely, but must be read always at the same standard temperature, for example, 20° C., since there is an appreciable temperature effect, for example, +1% error for a 4° C. rise in the case of cobalt sulphate (green filter). Sometimes "flaking" may occur owing to some slight action on the glass of the bottle. The solutions should not be filtered in this case, but should be carefully decanted. If a lamp or photo-cell has been changed, a check with these solutions will indicate whether a calibration curve previously obtained for a specific chemical determination will have to be replotted. It is most important to replot if the values obtained with the copper and cobalt sulphate standards differ from those originally obtained.

The stock bottles containing the copper and cobalt sulphate crystals used to prepare the original solutions should be set aside for making up these standards only. In this way standards may be exactly reproduced over a period of many years.

Effect of Temperature.

Although it is well known to the physicist, few chemists apparently realize the possible effect of a change in room temperature on the accuracy of their results. As mentioned above, the effect on the cobalt sulphate solution is appreciable under room temperature conditions operating in this country, though, fortunately, the end colour in most biochemical estimations is not nearly so sensitive. If the methods given by King[2] are used, some estimations—for example, those of hæmoglobin (as oxyhæmoglobin), bilirubin (van den Bergh method) and phosphatase (phenyl phosphate method)—have a negligible temperature error, even for the most accurate work; whereas others—such as those for glucose (arsenomolybdate method), urea (Nessler's method) and thiocyanate (ferric nitrate method)—are affected by temperature change. For most clinical work this error is unimportant, but it may be disturbing if one is trying to reproduce results with standards or check calibration curves. Hence the desirability of the inclusion of a standard solution with the unknowns in routine procedure.

In passing it should be noted that room temperatures in Australia are often much higher than in those parts of Europe and America where most of the clinical biochemical methods were developed. This must be remembered in performing some estimations, such as those for potassium (cobalti-nitrate method), proteins and urea, and other determinations based on estimation of ammonia by Nesslerization.

The preparation and addition of the sodium cobalti-nitrate reagent and washing of the precipitate would be performed with ice cooling to prevent decomposition of the reagent. Nessler's reagent should be added to solutions containing ammonia cooled to 11° C. for consistent results, otherwise precipitates form which make photometry impossible.

Calibration for a Particular Determination.

With the visible type of colorimeter (for example, the Duboscq) it is customary to prepare a standard which has been through the same procedures as the unknown and to compare them. While it is not always necessary with the photoelectric colorimeter to run a standard with the unknown, it is always desirable, particularly if the colour reactions take time to develop or fade quickly. Sometimes the reagents or final colours are unstable or the final colour is temperature-sensitive; and until experience has shown that the standards give reproducible density values, one standard of value close to the unknown should be used with each run, if possible, even in those cases in which the calibration curve has been plotted.

A calibration curve may be constructed as follows. A series of standard solutions are prepared, and aliquots of them, together with a blank, carried through the specified procedures. A filter of the complementary colour to that of the solution being measured should then be used and the density values obtained for each of the standards, the "blank" being used to set the galvanometer at zero density. (For a red solution use a green filter, for a yellow a blue filter, for a blue or green a red or orange filter.) Usually the filter giving the highest density readings for the particular solution is the correct one to use. (Ideally the absorption curve of the solution should be obtained from the literature or with a spectrophotometer, and a filter selected with a transmission peak corresponding to the absorption peak of the solution.) The results should then be plotted on ordinary graph paper, concentration horizontally against density reading vertically. This should give a curve which is, or very nearly is, a straight line passing through the origin. If this is not so, other likely filters should be tried and the one giving the highest readings with the best linearity chosen. With the D.G. spectrophotometer density values should be taken every 10mμ over the range where the peak of the absorption curve is likely to be, the results plotted and the peak determined by inspection. This peak value should then be set for all subsequent determinations. On no account should published calibration curves be used, since these may be quite different for individual instruments. These curves are published for guidance only, to give some indication of the type of curve to be expected with a given instrument. Calibration curves should be checked periodically if a standard is not run regularly.

TABLE II.
Fault Finding.

Symptom.	Possible Cause.	Correction.
No meter deflection when instrument switched on.	Shutter closed or zeroing cell in position.	Open shutter or remove cell.
	Burnt-out lamp.	Replace and recalibrate instrument if necessary.
	Fault in wiring of lamp circuit or meter circuit.	Repair.
	Broken galvanometer suspension, especially with lamp and scale type of instrument.	Send instrument to a meter repair workshop.
	Fault in main switch or cable.	Consult electrician.
Erratic meter movement.	Insufficient warm-up time.	Allow three or four minutes for warm-up.
	Bad connection in lamp circuit.	Clean and tighten connections of battery. Screw in lamp firmly or clean contacts to it.
	Major changes in line voltage or frequency beyond capacity of C.V. transformer.	Investigate causes with the help of supply engineer if persistent; in some localities C.V. transformers may be unsuitable.
	Failing lamp (sometimes difficult to detect).	Replace.
	Bad connections in meter circuit.	Tighten all connections. Clean, if necessary, connections to photo-cell.
	Worn potentiometer.	Replace.
	Meter needle touching face.	Send to meter repair workshop.
	Sticking diaphragm.	Grease.
	Battery below charge.	Recharge.
Inability to set meter on 100% transmission.	Failing photo-cell.	Replace and recalibrate if necessary.
	Failing lamp.	Replace and recalibrate if necessary.
	Battery below charge.	Recharge.
Failure to obtain correct reading with standard solutions.	Photo-cell fatigued.	Replace.
	Solutions not at standard temperature.	Bring to standard temperature.
	Filters deteriorated.	Replace.

A very convenient method for drawing curves is as follows. The points of the curve are plotted on graph paper, a sheet of cardboard is placed underneath, and the points are pricked through with a needle. The holes in the card are "crossed" with a pencil and the curve is formed with a pair of scissors by cutting from one cross to the next as smoothly as possible. Slight irregularities in the edge are removed by rubbing down with sandpaper, and the "template" is then used with a pencil or ruling pen to join the points on the graph paper. In this way very smooth accurate curves can be drawn.

If the curve is linear, it is possible to obtain a factor by which subsequent values obtained on the colorimeter can be multiplied. Thus, for example, if one millilitre of urine is to be used for the determination of urinary creatinine, and if in preparing the linear curve it has been found that one millilitre of a standard solution of creatinine (one milligramme per millilitre) carried through exactly the same procedures and with the same dilutions has given a density reading of 0·56 for the particular instrument, filter and absorption cell used, the calculation would be as follows:

$$\text{Urine creatinine in milligrammes per 100 millilitres} = \frac{\text{Reading unknown}}{\text{Reading standard}} \times 1{\cdot}0 \times \frac{100}{1}$$

$$= \frac{\text{Reading unknown}}{0{\cdot}56} \times 100$$

$$= \text{Reading unknown} \times 179$$

So 179 becomes the factor by which subsequent readings are multiplied. If it was found that this factor was quite reproducible, it could be used for all subsequent work, provided that occasionally a fresh standard was run and the value had not altered.

Choice of Comparison of Unknown with Standards.

The question arises of when a calibration curve, a standard or a factor should be used.

1. Calibration curves should be used with compounds like oxyhæmoglobin when it is virtually impossible to check against a standard of the same substance each time. Here an artificial standard, such as a neutral glass filter or a cobalt sulphate solution, is a valuable check.

2. Calibration curves should also be used when the curve is far from linear, though here, too, it is desirable to run a standard of value close to the unknown as a check on results.

3. A series of standard solutions should be used when the reagents or final colours are unstable or when maximum accuracy is required. It must be remembered that standard solutions (particularly dilute standards) are sometimes unstable and should be freshly made up from time to time.

4. A factor may be used when reagents and colours developed are dependable and the curve is linear.

Conclusion.

Often the photometric stage of a procedure can be the one which will most critically influence the accuracy of the determination. Attention to the details offered in these notes will give the chemist confidence in his results and do justice to his skill in performing the often involved procedures leading up to the final measurement. It is often easy to get an answer, not always so easy to get the correct answer.

Summary.

1. The components of the simple photoelectric colorimeters most widely used in Australian clinical laboratories are discussed in detail, with particular reference to defects likely to develop.

2. Methods are discussed for the standardizing of these instruments for clinical work and the prevention and correction of faults that may occur in practice.

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Bibliography.

(1) Delory, G. E. (1949), "Photoelectric Methods in Clinical Biochemistry", Hilger and Watts.

This is the best general book on the subject.

(2) King, E. J. (1951), "Micro-analysis in Medical Biochemistry", J. and A. Churchill.

This and the preceding reference book tend to oversimplify and summarize some procedures and should be read in conjunction with more detailed methods.

(3) Hepler, O. E. (1950), "Manual of Clinical Laboratory Methods", C. C. Thomas, United States of America, and Blackwell Scientific Publications, London.

This manual gives some photoelectric methods and is a very thorough and up-to-date volume covering all phases of clinical laboratory work. It is well worth having in any clinical laboratory.

(4) Fister, H. J. (1950), "Manual of Standardized Procedures for Spectrophotometric Chemistry", Standard Scientific Supply Corporation, New York.

This is a detailed but very expensive loose-leaf manual for the more critical clinical user of photoelectric colorimeters and spectrophotometers.

(5) Mellon, M. G. (1950), "Analytical Absorption Spectroscopy", John Wiley and Sons, New York, and Chapman and Hall, London.

The most complete and up-to-date book on the theory and application of colour measurement to chemical analysis. It will be found too theoretical for the average reader, but invaluable to those who wish to study the fundamentals of the subject.

(6) West, W. (1946), "Colorimetry, Photometric Analysis and Fluorimetry", in "Physical Methods of Organic Chemistry", Volume II, Interscience, New York.

A physicist's exposition of colorimetry dealing mainly with instruments and principles.

(7) "Taking Care of Your Battery", Exide Batteries of Australia.

This is available free of charge on application. It contains valuable information on the care of batteries.

Reports of Cases.

A CASE OF GAISBÖCK'S DISEASE (POLYCYTHÆMIA HYPERTONICA).

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Polycythæmia rubra vera has been defined by Parkes-Weber and Bode (1929) as follows: "A disease or morbid condition characterized by well marked persistent relative and absolute polycythæmia (increase in the number of red corpuscles), due to an excessive erythroblastic activity of the bone marrow, which in the present state of knowledge appears to be the primary morbid factor in the condition; it is characterized likewise by persistent increase in the so called blood viscosity and total blood volume and often by a cyanotic appearance of the patient and usually, if not always, by an easily felt enlargement of the spleen."

As well as an increase in the total red cells in the blood, there is nearly always, according to Whitby and Britton (1946), an increase in the leucocytes and platelets; the blood picture is, therefore, a mirror of the activity in the bone marrow, where the erythroblastic and leucoblastic tissues as well as the megakaryocytes are increased—a panmyelosis. A normal bone marrow finding does not, however, rule out a diagnosis of *polycythæmia vera*, but is a rare occurrence in that condition.

Engorgement with blood is the main cause of any splenic enlargement, but hyperplasia of the pulp occurs in which there are areas of erythropoiesis. The spleen is not always

enlarged, and Fairley (1945) quotes Tinney, Hall and Giffin (1943) as stating that, in a series of 163 cases of *polycythæmia vera*, the spleen was easily palpable in only 107 (66%).

With reference to hypertension in this disease, Whitby and Britton (1946) state that it is in the later stages that the blood pressure rises, normal pressure in the early stages being maintained by a compensatory dilatation of the capillaries. Taquini, Suarez and Villamil (1949) consider that hæmodynamic adaptation takes place by a great increase in the blood volume and vascular bed with considerable arteriolar-capillary dilatation, so that a normal peripheral resistance is maintained in spite of increased blood viscosity. Arterial pressure and work thrown onto the left ventricle are thus kept within normal limits.

Gaisböck (1905) described a condition in which polycythæmia was associated with high blood pressure and in which there was no splenomegaly. It occurred usually in the sixth decade and was characterized by a cyanotic appearance, arteriosclerosis and renal disease, and often some cardiac hypertrophy, and was called *polycythæmia hypertonica*. Whitby and Britton (1946) state in this respect that arteriosclerosis is usual in *polycythæmia vera*, but, although there is fibrosis of the heart muscle, cardiac hypertrophy is rare.

Many authorities, among whom are Wintrobe (1951) and Davidson (1937), regard Gaisböck's disease as merely *polycythæma vera* with secondary high blood pressure; but others, such as Whitby and Britton (1946) and Parkes-Weber (1929), consider that there is such an entity. The last-mentioned thought that polycythæmia in patients with high blood pressure was more common than suspected, while Whitby and Britton (1946) suggest that such drugs as phenylhydrazine should not be used for fear of accentuating the renal damage in these cases.

The difficulty in accepting Gaisböck's ideas lies in showing conclusively that any hypertension associated with polycythæmia antedated the blood changes and could not have been caused by the effect of such changes on the blood vessels. Although adaptation of the hæmodynamics may take place in the early stages without rise of blood pressure, in *polycythæmia vera* it is reasonable to suppose that this may break down in later years and hypertension follow. At the same time, in the fifty to seventy years age group, hypertension is so common in the community that the association of this with polycythæmia may be fortuitous and the conditions unrelated. Again, in many cases in which arteriosclerosis has existed with hypertension for some time, kidney changes may occur, the late pathology of which may be similar to those of the chronic stage of primary renal disease. According to Gaisböck's definition, any of the above conditions could be labelled *polycythæmia hypertonica* provided no spleen was palpable. It has been seen, however, that neither the absence of splenomegaly nor a normal bone marrow reaction would be against a diagnosis of *polycythæmia vera*; so these are of no help in proving Gaisböck's contention. Nevertheless, in certain cases, polycythæmia may follow hypertension and not *vice versa*, and this fact rather than the absence of splenomegaly may distinguish the series of cases Gaisböck described, especially where renal pathology is present. To these cases the name *polycythæmia hypertonica* could well be applied.

Clinical Record.

The following history relates to a case of hypertension of known ætiology preceding polycythæmia. The patient, a male, aged forty-two years, had had no serious illnesses previously. There was no family history of polycythæmia, but his mother died after an unspecified renal operation.

In 1942 he was found to have albuminuria, and tonsillectomy was performed as the result.

In 1944 hypertension developed, and after an attack of hæmaturia in 1946 cystoscopy was carried out. He was told that an hereditary condition was responsible for the hæmaturia.

At the end of 1950 a right hemiplegia developed, followed by venous thrombosis of patchy distribution in the left leg. Vein biopsy yielded normal findings. While he was in hospital at this time (from January 29, 1951, to April 4, 1951) pneumonia supervened, but the chest X-ray appearances on June 5, 1951, were normal.

On July 19, 1951, no further vascular accident had occurred, but his legs were still œdematous, although the hemiplegia had lessened considerably. He looked well, but hæmaturia was noted transiently on three or four occasions without scalding or pyrexia. The blood pressure was now 200 millimetres of mercury, systolic, and 130 millimetres, diastolic, but there was no cardiac enlargement, and the retinal vessels were normal. Resistance was felt in the right hypochondrium, but no definite abdominal mass.

Blood examination showed the hæmoglobin value to be 106%, the number of erythrocytes 6,100,000 per cubic millimetre and the number of leucocytes 10,400 per cubic millimetre. The red cells were of normal appearance. The leucocytes were distributed as follows: neutrophile polymorphonuclear cells 72%, lymphocytes 21%, eosinophile cells 2%, large monocytes 5%. The bleeding and clotting times were within normal limits, but much albumin was present in an acid urine, which contained many red and white blood cells, as well as granular and blood casts. The blood urea content was 109 milligrammes per 100 cubic centimetres, while the urea clearance was 26·5% and urea concentration test results were also poor.

The hypertension was regarded as being of the malignant essential type or of renal origin, possibly following acute nephritis in 1942.

In early September of 1951, the blood pressure was 160 millimetres of mercury, systolic, and 120 millimetres, diastolic, and on November 9, 1951, the hæmoglobin value had risen to 144%, and the number of red cells to 8,150,000 per cubic millimetre. The patient felt tired and dyspnœic on exertion, but had no nocturnal dyspnœa, and the œdema of his legs had subsided somewhat. A venesection (amount unknown) was performed at this stage.

On November 19, 1951, the hæmoglobin reading was 132% (19 grammes of hæmoglobin per 100 cubic centimetres), while the number of erythrocytes had reached 9,000,000 per cubic millimetre. The white cell count, which included a differential count, was normal, as were the platelets. A bone marrow smear examination showed that the cellularity had increased, and the pathologist's comment was that the hyperplasia was in the erythroid elements alone, a finding compatible with a diagnosis of *polycythæmia vera* but not the common form of change in that condition. After further venesections, the blood pressure on December 6, 1951, was 144 millimetres of mercury, systolic, and 120 millimetres, diastolic, and there was no cyanosis of skin or mucous membranes. Retinal arteriosclerosis was present with some nipping of the veins but no hæmorrhages or exudate. No enlarged glands were noted at this examination, while the chest was clinically clear. The liver edge was palpable three fingers' breadth below the right costal margin, but the spleen was not palpable. Enlargement of left upper abdominal glands was suspected, and there was a fullness over the left upper lumbar region of the spine. A large right inguinal hernia was also present. After another venesection, radioactive phosphorus (P^{32}) was given intravenously on January 10 and 16, 1952 (three millicuries on each occasion). On February 4, 1952, the hæmoglobin value was 102%, and there was a thrombosis in the right cubital fossa. On March 17, 1952, further hæmaturia occurred, and cystoscopic examination showed prostatic enlargement with dilated bleeding veins over the bladder and prostate. No blood flowed from either ureter.

Fever, shivers and sweats on March 27, 1952, followed bouts of epigastric pain five days and three days previously. A few basal crepitations were heard, slight cardiac enlargement was noted, and the blood pressure was 148 millimetres of mercury, systolic, and 110 millimetres, diastolic.

He was admitted to hospital on April 4, 1952, with pain in the right side of the chest, the blood pressure then being 140 millimetres of mercury, systolic, and 100 millimetres, diastolic, with no cardiac abnormality. Dullness to percussion detectable at both lung bases posteriorly, with diminished breath sounds and vocal resonance and fremitus at these areas, was associated with similar findings in the left axilla. The liver edge was palpable two fingers' breadth below the right costal margin, but no spleen was felt. The ocular fundi were within normal limits.

On April 7, 1952, the splenic tip became palpable, and it was thought that the abdominal pain might have been due to a splenic infarct.

Renal function had deteriorated, the fasting blood urea content being 195 milligrammes per 100 cubic centimetres and the urea clearance 15% of normal.

The hæmoglobin value was 112% (16 grammes per 100 cubic centimetres) with an erythrocyte count of 5,650,000 per cubic millimetre and a leucocyte count of 8700 per cubic millimetre; the platelet count was 452,000 per cubic millimetre. The red cells were normocytic and normochromic, while there was a neutrophile leucocytosis. Many red and pus cells were in the urine, but no bacteria.

A chest X-ray examination showed a diffuse loss of translucency in the first right intercostal space laterally which was consistent with early segmental pneumonitis.

The result of a Mantoux test (dilution 1:1000) was negative after forty-eight hours, as was a blood culture after five days. The fæces contained no enteric pathogens, and the results of agglutination tests against these, *Brucella abortus* and the common typhus organisms were negative.

On April 30, 1952, readmission of the patient to hospital was necessitated by retrosternal pain, which had occurred thirty-six hours previously, lasted an hour and was associated with shortness of breath. It recurred on moving about. He was mildly pyrexial with a pulse rate of 120 per minute. The specific gravity of the urine was 1.008, but no albumin was present. The blood pressure was 130 millimetres of mercury, systolic, and 100 millimetres, diastolic, but the heart was not enlarged and its sounds were normal. The lungs were clinically normal, and indefinite swellings were palpated under the right and left costal margins. His fingers were clubbed and cyanosed.

His retrosternal discomfort was thought to be due to cardiospasm, which with his headache formed part of a "tension" syndrome. Electrocardiograms were physiological in type, but on May 2, 1951, the hæmoglobin value was 126% (18 grammes per 100 cubic centimetres) and the erythrocyte count was 6,380,000 per cubic millimetre. The cells were normocytic and normochromic, while a white cell count of 4550 per cubic millimetre was differentially normal. Platelets were plentiful.

An X-ray examination at this time showed no gross lung changes and no gross cardiac disproportion, while no organic lesion was demonstrated radiologically throughout the stomach, duodenum or terminal part of the œsophagus.

On May 16, 1952, a blood culture produced no growth.

On June 5, 1952, he was given a further three millicuries of P^{32} intravenously, but on July 29, when first examined as a patient of the Royal Melbourne Hospital, he was unable to work and had an ache in the right loin. His colour was dusky but not definitely cyanotic. The blood pressure was 160 millimetres of mercury, systolic, and 120 millimetres, diastolic, and the heart sounds were clear, while the lungs were clinically normal. The liver edge was palpable on deep inspiration, and what was thought to be the spleen could be felt three fingers' breadth below the left costal margin. The right kidney was palpable as an enlarged irregular mass occupying a large part of the right loin. The peripheral circulation was adequate, although signs of a previous thrombosis were present in the left leg.

The possibility of the kidney being polycystic was considered, and a flat X-ray film suggested that the right kidney at least was grossly enlarged. An excretion pyelogram on August 20 showed no dye in films one and a half hours after injection, and the kidneys were apparently very large. A tiny calculus was probably present in the left kidney. It was then thought that what was previously called spleen was almost certainly an enlarged left kidney.

On August 18 the hæmoglobin value was 112% (16·5 grammes per 100 cubic centimetres) and the erythrocytes numbered 5,500,000 per cubic millimetre. The leucocytes numbered 6500 per cubic millimetre.

His condition had deteriorated by September 9, nausea, headaches and cramps were worrying him, while he was more dyspnœic and had urinous breath.

Further hæmaturia occurred on September 23, and hypogastric pain was accompanied by melæna, nose bleeds, backache and nocturia. The blood pressure on September 30 was 150 millimetres of mercury, systolic, and 110 millimetres, diastolic, and the fæces were still dark. On October 31 the hæmoglobin value was 97% (14·3 grammes per 100 cubic centimetres) and the erythrocytes numbered 5,800,000 per cubic millimetre. The leucocyte count was 5500 per cubic millimetre, while the blood urea content was 180 milligrammes *per centum*. The renal function was extremely poor. His condition deteriorated steadily, and on February 24, 1953, he was dyspnœic, tremulous and vomiting. There was no cardiac enlargement or any sign of cardiac failure. The blood pressure stood at 145 millimetres of mercury, systolic, and 110 millimetres, diastolic, and, although the tumour in the left loin was thought to be renal, the tip of the spleen was probably palpable as well. On March 19 the hæmoglobin level was 105% (15 grammes per 100 cubic centimetres), and the erythrocyte count was 5,800,000 per cubic millimetre. The leucocytes numbered 6500 per cubic millimetre.

On April 14 he complained of pain in the left side of the face present for two weeks, and he was found to have left facial palsy of the lower motor neuron type. Abdominal masses were felt on the right and left sides, and the blood urea level was 266 milligrammes *per centum*.

He was admitted to hospital for the last time on April 25, with severe vomiting and itching of the skin, rapidly increasing dyspnœa, severe headache and loss of appetite and weight. The blood pressure was 160 millimetres of mercury, systolic, and 120 millimetres, diastolic, and the heart was clinically enlarged. The urine, which had a specific gravity of 1·010, contained a two-thirds deposit of albumin on boiling, and the blood urea level was 236 milligrammes *per centum*.

His condition rapidly deteriorated, and death, due to uræmia, occurred on May 3, 1953.

A post-mortem examination showed the following relevant conditions. Old fibrinous adhesions were present over the right lung at its base and laterally. The lungs were congested but no consolidation was present. The heart, pericardium and great vessels weighed 325 grammes. The pericardial sac contained 10 cubic centimetres of clear fluid, and the cardiac muscle was pale but firm. The line of closure of the mitral valve was thickened and roughened without obvious vegetations. The aortic valve showed slight atheroma, as did the abdominal aorta. The stomach was dilated and contained innumerable acute pin-point ulcers over the acid-bearing area extending to just beneath the submucosa. There was no fresh blood in the stomach. The liver was pale, smooth and firm and weighed 1800 grammes, just above normal size. The gall-bladder was packed with rhomboidal calculi, and its wall was slightly fibrous.

The spleen was firm and dark red. It weighed 223 grammes, only slightly over normal size.

The right and left kidneys weighed 1900 and 2050 grammes respectively, or ten times normal size. They consisted almost entirely of innumerable cysts, 0·5 to 6·0 centimetres in diameter, which contained mostly clear yellow fluid. Little, if any, kidney tissue was present, but the ureters were normal. The bladder mucosa was œdematous, and numerous submucosal clots were present, while the mucosa itself was raised in papilliferous folds.

The cerebral vessels were only slightly atheromatous. In the cuneus of the right occipital lobe there was an area of soft brain tissue, in which were present some petechial hæmorrhages resembling thromboses of four to five days' duration. Both hemispheres were normal, and no old thromboses were evident. The mid-brain and cerebellum were normal.

Discussion.

The patient was undoubtedly suffering from polycythæmia if the standards of Price Jones (1931) are accepted. He states (as quoted by Fairley, 1945) that in England the range in health calculated from the standard deviation of the distribution of a large series of observations is from 5,100,000 to 6,350,000 erythrocytes per cubic millimetre in adult males; while in their capillary blood the observed limits for hæmoglobin were from 96% (13·2 grammes per 100 cubic centimetres of blood) to 116% (16·0 grammes per cubic centimetre), the possible limits calculated from *plus* and *minus* three times the standard deviation being 96·6% (13·3 grammes per 100 cubic centimetres) and 117·2% (16·2 grammes per 100 cubic centimetres).

Whitby and Britton (1946) give the normal range for the adult male as from 14 to 17 grammes of hæmoglobin per 100 cubic centimetres of blood, and the upper range of erythrocytes as 6,400,000 per cubic millimetre, an increase above 6,500,000 per cubic millimetre being abnormal. In polycythæmia vera red cells usually range from 7,000,000 to 12,000,000 per cubic millimetre, and the hæmoglobin value from 120% (16·5 grammes per 100 cubic centimetres) to 160% (22·1 grammes per 100 cubic centimetres); the leucocytes usually vary from 10,000 to 40,000 per cubic millimetre with from 75% to 85% of polymorphonuclear cells. Rare examples of low leucocyte counts in this disease have been recorded by Parkes-Weber and Bode (1929).

In the present case, therefore, the fact that there was an increase in white cells in the peripheral blood on three occasions only, and that no increase in platelets was recorded, *plus* the fact that the bone marrow examination failed to show a panmyelosis, is not against a diagnosis of *polycythæmia vera*, but the findings recorded are not the typical ones. The hypertension was without doubt related to the polycystic kidneys, and no question, therefore, arises of the polycythæmia predisposing to the hypertension, or of the latter existing coincidently as essential hypertension. It is not necessary either to invoke any other renal cause for the hypertension or to suggest that the renal pathological condition was due to hypertension. The separate existence of two such uncommon diseases as polycystic kidneys and *polycythæmia rubra vera* in this patient is so unlikely that he can, therefore, be reasonably said to have had Gaisböck's disease or *polycythæmia hypertonica* existing as a definite entity, inasmuch as hypertension of known renal ætiology preceded polycythæmia without splenomegaly.

His age at death was rather lower than in Gaisböck's group, however, and was obviously related to the kidney disease. The absence of splenomegaly is of doubtful significance in making such a diagnosis, as shown by Fairley; but this clinical history indicates that *polycythæmia hypertonica* can be accepted as an entity, although probably rarer than Gaisböck suggested. On the other hand, among patients of the older age groups, when there is no increase in white cells and platelets in the peripheral blood and bone marrow is not typical, it may be very difficult to show that the hypertension did not precede the polycythæmia, if both conditions are present when the patient is first examined. It is not unreasonable to suggest, therefore, that some of these cases also are examples of *polycythæmia hypertonica*; and when doubt exists, efforts should be made to exclude renal and other causes for the hypertension.

Other interesting aspects of the course of this patient's disease are the hæmaturia and the melæna. The dilated vesical and prostatic veins were probably associated with the polycythæmia as an attempt to cope with the increased blood viscosity, but one could have been pardoned for assuming that the blood was renal in origin and not vesical once the possibility of polycystic kidney disease was thought likely. Bowel hæmorrhages are associated with uræmia, but in this case the possibility of duodenal ulcer had to be thought of, as this condition frequently complicates *polycythæmia vera*.

As far as treatment is concerned, it would appear that this patient benefited by that given; but obviously the prognosis cannot be altered in such cases, and it is doubtful whether the patients should be managed in the same way as those with *polycythæmia vera*. Perhaps the more frequent use of venesection may be preferable to P³² therapy. The latter could be reserved for patients with initial very high red cell counts.

Acknowledgements.

Thanks are expressed to Dr. R. Kaye Scott and Dr. Bruce Robinson, as well as to the medical staff of the Royal Melbourne Hospital, for the use of the early clinical notes on this patient.

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A CASE OF THALLIUM POISONING COMPLICATING PREGNANCY.[1]

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RECENTLY considerable publicity has been given to thallium poisoning, and many cases have been recorded and described in the lay Press; but the disease is not a new one.

As long ago as 1934 Munch published a very complete review of 778 cases of thallotoxicosis culled from world literature, and since then sporadic cases have been reported in many journals. Recently Allsop (1953) published a detailed study together with 18 case reports.

Toxic effects of the drug include fatigue, gastro-intestinal disturbances, anorexia, vomiting and diarrhœa, disorders of the central nervous system, polyneuritis, encephalitis, retrobulbar neuritis, optic atrophy and psychosis, and the specific clinical feature—epilation.

Munch's review covered 778 instances of thallium poisoning as follows: (i) Industrial poisoning, 12 cases with no deaths, but three persistent disabilities, albuminuria in two cases and double optic atrophy in one case. (ii) Poisoning in children following the proper use of thallium acetate as a depilatory, 447 cases with eight deaths. The dosage was eight milligrammes per kilogram. (iii) Poisoning due to the improper use of thallium acetate as a depilatory, 33 cases with 22 deaths, 18 due to overdosage and four to the administration of the drug to ill or undernourished children. (iv) Poisoning following the external application of a depilatory ointment, 50 cases with no deaths. (v) Miscellaneous thallium poisoning, 153 cases

[1] This patient was shown at a meeting of the New South Wales Branch of the British Medical Association held on December 3, 1953, at The Saint George Hospital.

with one death. (vi) Toxicological poisoning, 53 cases with 10 deaths. (vii) Accidental poisoning by ingestion of a rodenticide, 21 cases with five deaths.

Information concerning the minimal lethal dose was given. Doses varying from 5·5 milligrammes per kilogram to 7·5 milligrammes per kilogram caused the death of four sick children in from thirteen to twenty-six days. A dose of eight milligrammes per kilogram caused toxic symptoms in 219 healthy patients and the death of six of them. On the other hand, a total dosage of 900 to 1200 milligrammes failed to cause death in one adult, but a further 600 milligrammes caused retrobulbar neuritis, dementia and death. Doses varying from 85 to 125 milligrammes per kilogram caused death in from twenty-four hours to five days in several cases.

In spite of the large number of cases described by Munch and by others, I have been able to find no record of thallium poisoning complicating pregnancy, nor any information concerning the effect of thallium on the fœtus.

Clinical Record.

Mrs. H., a *multipara*, aged thirty-one years, pregnant for the fourth time and due for confinement in June, 1953, returned from a holiday on January 4, 1953, complaining that for several days she had been vomiting and had had pains on micturition and numbness followed by a burning pain in the legs. Treatment with sulphonamides and potassium citrate was instituted on January 9, with relief of the urinary symptoms but not of the pain in the legs. On January 28 *Bacterium coli* was cultivated from a catheter specimen of urine. Vomiting recommenced on February 9, and her hair began to fall out. In addition she had difficulty in micturition and some disturbance of bladder sensation. On February 16, when her presenting symptoms were vomiting, difficulty on micturition, muscular weakness and falling hair, she was admitted to the Saint George Hospital. One of her three children was also admitted to hospital with alopecia.

On examination of the patient she was seen to be five months pregnant. When she was put in the sitting position in bed, a striking amount of shed hair covered the sheet. Significant findings on physical examination were as follows: Tachycardia was present, and a systolic murmur was heard at the pulmonary area. The blood pressure was 140 millimetres of mercury, systolic, and 90 millimetres, diastolic. Motor weakness of the legs, arms and face was present, with cutaneous hyperæsthesia of the feet, legs and abdominal wall, and increased deep reflexes; the plantar reflex was flexor in type on both sides. The patient's mind was clear. The urine contained a heavy cloud of albumin. A twenty-four hour specimen of urine, tested on February 17, contained 15 milligrammes of thallium per litre.

Treatment was commenced with BAL, two cubic centimetres being given every six hours. As vomiting continued after her admission to hospital, an intravenous infusion of dextrose in saline was instituted, 750 cubic centimetres being given *plus* an amount equal to the volume of vomitus lost and the urine passed in each twenty-four hours; 0·7 gramme of sodium thiosulphate was given intravenously. On the same day it was decided to institute treatment with iodide, and 20 cubic centimetres of 12% sodium iodide solution were given intravenously, and the dose was repeated daily thereafter until on February 22, vomiting having ceased, it was possible to commence oral therapy with potassium iodide. The dosage of potassium iodide was 30 grains per day, increased gradually to 60 grains per day.

The general improvement in the patient indicated by cessation of vomiting was accompanied by a fall in the urinary excretion of thallium to nine milligrammes per litre on February 20.

Treatment was instituted for vaginal moniliasis on February 20. Four days later, plaster boots to correct foot drop were put in use. BAL therapy was suspended on February 25. The following day a urinary infection developed, with pyuria and hæmaturia. This was controlled by sulphonamides. On March 3 the urinary thallium excretion was 1·8 milligrammes per litre. On March 7 cyanosis and dyspnœa appeared, and it was thought that it might be necessary to use a respirator, as the patient's respiration was very shallow. However, improvement occurred and this was avoided. By March 16 there was some improvement in motor power.

At this time, Mrs. H. was six months advanced in her pregnancy, but had felt no fœtal movements since her admission to hospital, nor had any movements been detected by any observer. (She had reported quickening in the out-patient department on January 9.) As the fœtus was thought to be alive (faint heart sounds of normal rate had been noted by some of those who examined her, although electrocardiographic confirmation could not be obtained), an X-ray examination of the abdomen was carried out. No X-ray evidence of fœtal death was detected. The possibility of fœtal paralysis by thallium which had passed across the placental barrier was considered.

By March 20 the patient was able to turn in bed. The gradual steady improvement was interrupted in the last week of March by an episode of pulmonary collapse, for which "Carbogen" inhalation was necessary. Diarrhœa with some fæcal incontinence continued to be troublesome. This symptom had been in evidence since March 19. During the ensuing weeks bacteriological examination of the stools revealed no pathogens. On March 28 the urinary thallium excretion was 0·12 milligramme per litre.

On April 9, when she was thirty-one weeks pregnant, the first faint fœtal movements were felt.

On April 16 the patient was allowed to sit up in a chair. Tachycardia finally ceased about the middle of May, at which time her hæmoglobin value was 11·5 grammes per 100 cubic centimetres.

The question of induction of premature labour to achieve an easy delivery was considered; but as there was no certainty that the fœtus was not suffering from motor weakness, including weakness of respiratory muscles, it was thought that it would be in better condition to survive if the pregnancy was allowed to proceed to term.

On May 21 the urine was free of thallium.

On June 10 the patient came into labour and was delivered of a full-term baby. The labour, in spite of a frank breech presentation of the fœtus and considerable residual weakness of the maternal abdominal muscles, was completed in one hour. It was followed by post-partum hæmorrhage, for which a blood transfusion was given.

The baby was small (weight five pounds 12 ounces). Movements were normally vigorous. The baby's hair was straight and black, and its length, one and a half inches, slightly exceeded that of the newly grown hair of the mother. There were no congenital abnormalities.

At the time of delivery thallium estimations were made on the maternal urine, the fœtal urine, the placenta and membranes and the liquor amnii. All these tests gave negative results. The progress of uterine involution and of lactation in the mother was normal. Her considerable asymmetrical flaccid weakness of the legs and abdominal wall gradually decreased with physiotherapy. By November she was able to walk unassisted, and she was discharged from hospital with some residual pareses.

Discussion.

By analogy with lead, it seemed possible that thallium poisoning might adversely affect the course of pregnancy and might injure the unborn baby. It is known that women suffering from lead poisoning are less likely to conceive and more likely to miscarry than normal women, and, should their pregnancy go to term, the babies are more likely to be still-born, and less likely, if born alive, to survive the neonatal period than are normal babies. It is known that thallium is universally distributed throughout the tissues of the body in cases of poisoning, and it might be suspected that it could be diffused across the placental barrier and poison the fœtus, although information to this effect could not be obtained from the literature. It was hoped that some positive evidence might

be obtained in this case, since the mother was severely poisoned, her paralysis was widespread and persistent, and the thallium output in her urine reached a high level.

The fœtal movements had been first noticed about the nineteenth week of pregnancy. Their disappearance during the illness and eventual return about the thirty-first week seem to suggest that the baby suffered some degree of paralysis, although chemical evidence in support of this was not obtained.

The fœtal heart sounds were first heard in March, and their rate was never greater than one would have expected in a normal fœtus. In the mother, however, there was pronounced tachycardia from the time of her admission to hospital until the middle of May.

The absence of tachycardia in the baby and the fact that the baby's movements were all normal and vigorous at birth, although the mother was still considerably paralysed, can be explained either by a concentration of thallium in the baby's tissues lower, as a result of placental screening, than in the mother's, or by the generally accepted theory that children are less susceptible than adults to the toxic effects of thallium. The presence of a good crop of hair on the baby's head at birth is not surprising, as the mother's hair was noted to be growing again on about March 5, in the twenty-sixth week of her pregnancy, and the normal fœtus can be expected to show hair at the twenty-eighth week.

This single case, then, suggests that when thallium poisoning occurs during pregnancy the child, as well as the mother, is poisoned, but is less severely affected. If the mother survives, the child will survive. If the poisoning occurs later in the pregnancy, the baby may still show paralysis at birth. It would seem also that if the mother's condition is improving, the induction of premature labour is better avoided. In the present case there seemed to be no loss of power in the uterine contractions, although some voluntary muscles in the lower limbs and abdominal wall were still paralysed.

Summary.

A case of thallium poisoning complicating pregnancy is described. The prognosis for the child is considered.

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VAGINAL HYSTERECTOMY WITH REMOVAL OF LARGE OVARIAN DERMOID CYST PER VAGINAM.

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Perth.

THE report of this case seems warranted because of the size of the dermoid cyst and the unusual method of its removal.

Mrs. V., aged fifty years, was admitted to hospital complaining of swelling of the feet and legs present for the past year. She had also noticed some increase in abdominal girth. Her menstrual history was one of regularity without menorrhagia or dysmenorrhœa till one year earlier, since when she had had periods of epimenorrhœa and oligomenorrhœa without excessive loss. She had three children, aged nineteen, fourteen and twelve years, her labours had been normal and she had had no miscarriages. Since the birth of the second child she had been conscious of some prolapse, which had increased considerably in recent months.

On examination, the patient appeared to be a healthy middle-aged woman. The abdomen was distended by a large cystic swelling arising from the pelvis and extending to the xiphisternum. It was not tender, and was mobile. Vaginal examination disclosed a third degree prolapse, the uterus being bulky. The cystic swelling occupied the pelvis. There was moderate œdema of the feet and ankles for which no general explanation could be found, the cardio-vascular and renal systems being normal.

In view of the rapidity of growth of the cyst and its mobility, the diagnosis appeared to be that of a large simple unilocular ovarian cyst, associated with and aggravating a procidentia.

As repair of the prolapse was necessary, it was thought possible that the performance of a vaginal hysterectomy would permit evacuation of the cyst and its vaginal removal. A posterior colpotomy was performed, which exposed a part of the cyst surface; this was punctured and about 180 ounces of fluid were evacuated. The glairy nature of the fluid indicated that a dermoid cyst was being dealt with. Vaginal hysterectomy was then performed, which permitted greater exposure of the cyst; from this were then scraped out some pounds of sebaceous material and fine hair. The further reduction in size then allowed the cyst, still weighing about two pounds, to be withdrawn. It was found to be growing from the right ovary, which was removed. The left ovary was small and normal. The peritoneal cavity was closed and the repair was completed in the usual manner. Convalescence was entirely uneventful.

Adhesions of the cyst wall to other abdominal organs would have necessitated an abdominal incision. Fortunately these were absent, and in view of the success of the experiment the unusual procedure appears to have been justified. The estimated weight of the cyst was 20 pounds.

CASE REPORT: "CORTOMYCIN" IN THE TREATMENT OF A CHEMICAL BURN OF THE EYE.

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Sydney.

MR. X., aged forty years, was splashed in the right eye by a mixture of ammonia and iodine. The eye was immediately irrigated with tap water and castor oil inserted.

He was examined by me next morning, when the eye was intensely injected, with chemosis and superficial sloughing of the conjunctiva, and the whole lower half of the cornea was denuded of epithelium. The pupil dilated evenly with homatropine drops.

"Butyn" sulphate drops (2%) were inserted, and the eye was given a thorough and prolonged irrigation with normal saaline lotion. Loose sloughing areas of conjunctiva were removed. He was ordered (i) a firm pad and bandage, (ii) bathing with tepid normal saline solution three times a day, (iii) atropine sulphate drops (1%) three times a day, and (iv) "Cortomycin" ointment two-hourly.

The next day the eye was very quiet with only a small stain on the cornea. The patient remained symptom-free thereafter, though a few spots of staining, visible only with the slit lamp, persisted on the lower half of the cornea for a month. His visual acuity on discharge from treatment was 6/6 when corrected with glasses. There was no symblepharon.

Discussion.

Since the introduction of cortisone used locally as drops or ointment in the eye, alkali burns have presented a much less formidable problem than previously. It is necessary to use an antibiotic as well, since the loss of epithelium provides entry for organisms, leading to corneal ulceration in the untreated eye.

The choice of neomycin as the antibiotic associated with cortisone in "Cortomycin" ointment is fortunate, for, to quote Finland (1953) commenting on the local use of bacitracin, polymyxin and neomycin, "their low irritating

and sensitising potential when used in this manner has made them especially useful for these purposes. Moreover, such usage is particularly appropriate because of the higher sensitising potential of most antibiotics that are used for systemic therapy". The same author praises the broad antibacterial range and rapid action of neomycin.

Combining cortisone and neomycin in the one ophthalmic tube simplifies treatment for the patient, who must often be confused by the different instructions for various drops, ointments and bathings.

Atropine is essential in the treatment of any severe corneal lesion, for iritis, which did not develop in this case, must always be considered as a possible complication.

The initial thorough irrigation and inspection to remove debris which might harbour more alkali are essential. Alkali burns carry a bad prognosis, because the severe inflammatory reaction is delayed. Damage to the corneal stroma occurs because of penetration beyond the epithelium as a result of saponification of the fatty epithelial barrier (Harley, 1953). The whole cornea may become opaque as a result of the severe keratitis that follows, and the patient may be off work for weeks or months with a painful inflamed eye.

Summary.

"Cortomycin" ointment and atropine were used locally for a chemical burn of the eye with rapid recovery.

Acknowledgements.

I wish to thank Andrews Laboratories, Limited, for supplies of "Cortomycin".

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Reviews.

Diseases of Metabolism: Detailed Methods of Diagnosis and Treatment. Edited by Garfield G. Duncan, M.D., with contributions by Walter Bauer, Hugh R. Butt, Abraham Cantarow, Garfield G. Duncan, Frank Alexander Evans, Ferdinand Fetter, Joseph M. Hayman, jnr., Angel Keys, Friedrich Klemperer, Rachmiel Levine, Edward H. Mason, Max Miller, John P. Peters, J. E. Rall, Rulon W. Rawson, Samuel Soskin, Tom D. Spies, Cecil Watson, Abraham White and Priscilla White; Third Edition; 1952. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10″ x 7″, pp. 1198, with 207 illustrations. Price: £7 2s. 6d.

THIS, the third edition of "Diseases of Metabolism", comes five years after the second. The new work has many commendable features, but tends to suffer the fate of similar text-books, namely, staleness of text. Many of the sections have not been altered in any way and are showing signs of being dated. One can appreciate that the labour of rewriting is enormous and beyond the capacity of busy men, but the growth of knowledge is no respecter of persons—"the moving finger writes and having writ moves on", and therefore while the information in this new edition is a very valuable storehouse, one cannot justifiably say that it is up to date along the whole front.

On the other hand it is refreshing to find that a radical change has been made in some sections, notably that on carbohydrate metabolism, which is now written by Soskin and Levine. The chapter is excellently written and the editor deserves great credit for including in his text-book the iconoclastic views of these authors on the nature of diabetes. The chapter on clinical aspects of diabetes has been completely rewritten and is a fund of information.

There are several additional chapters, including one on porphyrin metabolism by C. T. Watson and one on diabetes in childhood by Priscilla White. The chapter on disorders of the thyroid gland has been completely rewritten and brought up to date by Rawson and Rall.

The section on water balance by J. P. Peters has been partly rewritten, but now gives evidence of being patched. On page 339 two figures are given for the percentage of water in the body, 60% and 70%.

In the chapter on diseases of the kidney there is a new section on lower nephron nephrosis which in part would appear to have evaded editing. Among the more glaring examples is: "Unless the tubular damage has been too severe it is a reversible process and recovery can take place. The problem then is to attempt to prevent death in uremia before this has occurred." In this same chapter there is an *erratum* at the bottom of page 1046.

The use of cortisone and ACTH is considered in relation to various metabolic disorders, but there is no chapter dealing specifically with the collagen diseases.

The book has grown by some 150 pages, and there are extensive lists of references at the end of each section, and in addition a comprehensive author's index. It can be recommended for all requiring a broad knowledge of metabolic medicine and will be of great value for those working for higher degrees.

Anatomy and Surgery of Hernia. By Leo M. Zimmerman, M.D., and Barry J. Anson, Ph.D. (Med. Sc.); 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10½″ x 7″, pp. 384, with many illustrations. Price: £5 7s. 6d.

IT is good for a surgeon to read a book which informs him that early surgery is desired for every type of abdominal hernia, and how such surgery can always be successful. This book is jointly written by a surgeon and an anatomist, who combine surgical technique with a basis of structural physiology. Each chapter begins with a presentation of the general anatomy together with specific local descriptions of each particular type of hernia. Clear, full directions of each operation follow, with beautiful accompanying illustrations. Anson, of course, is well known for his Atlas, in which many of the illustrations appear.

Emphasis is laid on the fact that the operation for hernia demands experience and skill and should not be entrusted to young resident medical officers. The truss is condemned as a vicious and injurious agent and as having no place in the treatment of hernia, except in a very few strictly limited situations. The authors prefer the free transplantation of *fascia lata* as a flap or adjuvant patch to local suture repairs when indicated. The effect of papaverine on vascular spasm following the early vascular occlusion of strangulated bowel is favourably commented on, and in the doubtful case, may help in the decision as regarding resection.

Herniologists now agree that the saccular theory of the ætiology of adult indirect inguinal hernia is proven and that the sac is always of congenital origin. The preformed sac is a prerequisite, and sudden increased intraabdominal tension is always the exciting cause of protrusion, especially if unexpected. The interpretation of the role of trauma in causing herniation is of great help for the practitioner who is to undergo cross-examination, and the book is an authority which can be quoted and accepted.

The chapter on diaphragmatic hernia is one which British readers cannot readily accept. It ignores the work of Allison and Barrett in hiatus hernia, omits any reference to œsophageal reflux, and is generally disappointing in its approach to curative treatment and in discussion. One must criticize the prevailing American trait of not bothering with authorities, other than their own.

Clinical Cardiology. Edited by Franklin C. Massey, A.B., M.D.; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9″ x 6½″, pp. 1114, with 212 illustrations. Price: £7 5s. 3d.

THIRTY-THREE experts in their selected fields have combined to produce a text-book of "Clinical Cardiology" for graduates under the editorship of Dr. Franklin C. Massey, Assistant Professor of Medicine in the Hahnemann Medical College, Philadelphia. Each chapter begins with a page of biographical details of the author, including the place and date of his birth, from which it appears that sixteen of the contributors, including Professor Massey himself, who was born in 1917, are forty years of age or younger. Several of these are distinguished names in American medicine or surgery. It has been the avowed aim of the editor to achieve up-to-the-minute modernity: in fact, in one of his own chapters he recommends watching television as a useful adjunct to bed rest in the treatment of infarction of the heart. A certain basic knowledge by the reader is assumed: for instance, in the chapter on the treatment of congestive failure no precise directions are given for the dosage of digitalis, nor is its pharmacology discussed except as it relates to the electrocardiogram. However, the section on

the management of œdema in this chapter is very satisfactory and contains abundant practical detail. About one-tenth of the book is devoted to an excellent section on cardiac surgery; but this would seem to contain far too much description of surgical technique and too many illustrations of instruments and operations for a work intended for physicians; on the other hand its discussion of surgical indications in cardiac ischæmia is disappointingly brief. There is a further section of 55 pages on anæsthesia and surgery in the cardiac patient, which could well have been condensed. The section on neurocirculatory asthenia is written with the pen of experience and is likely to renew the interest of the physician who has not had much success with this condition. The section on arrhythmia (86 pages) sets out modern theory and practice as fully and clearly as we have seen it done. This chapter, like many others, would have been improved if the space at the beginning devoted to biographical notes had been used for a table of contents. The book is a heavy one, some two and a half inches in thickness, and well produced. One imagines that a second edition will be called for: with strict editorial discipline over the contributors in the allotment of space it could be better than the first.

The White Plague: Tuberculosis, Man and Society. By René and Jean Dubos; 1952. London: Victor Gollancz, Limited. 8" × 5¼", pp. 286. Price: 15s.

IT seems a pity that René and Jean Dubos could not have found some less forbidding title than "The White Plague", a long outmoded name, for their lively rendering of the tuberculosis story; for their book has qualities which might attract the interest of a much wider section of the public than that which has a personal or professional interest in the disease. Their style has a journalistic flavour and many of the chapters could well have appeared as "feature" articles in a week-end newspaper. This is not to suggest any shallowness of treatment or notable inaccuracy. The first section of the book, showing how the pervading presence of tuberculosis throughout society is reflected in all fields of literature, is like one of those old albums of pressed field flowers, which our grandparents so lovingly and patiently collected. Here are the stories of Chopin, of Keats, of the Brontës, of the Emersons and of many heroes and heroines of fiction. Another section deals with the causes of tuberculosis and the evolution of the germ theory before and after the discoveries of Villemin and Koch. A section on cure and prevention shows how modern methods have developed from empirical observation and scientific analysis and explores some of the many wrong turnings that have been taken. The final section traces the evolution of epidemics and the effects of the industrial revolution, of migration and of the growth of cities; it also deals with what is called the social technology of tuberculosis—fostering, exploiting and canalizing public goodwill in the campaign against the disease. The authors follow current Western orthodoxy in their absolute intolerance of the tubercle bacillus, and they look forward to the "conquest" of the disease. In looking backwards they shine an electric light into tallow-lit times: they see much suffering and sympathize with it without at all realizing contemporary solaces, and they refer reproachfully to the capitalist classes who climbed over sweating bodies to riches.

Planning Guide for Radiologic Installations. By the Committee on Planning of Radiologic Installations of the Commission on Public Relations of the American College of Radiology, Wendell G. Scott, M.D., Chairman; 1953. Chicago: The Year Book Publishers, Inc. 10¼" × 7¼", pp. 352, with many illustrations. Price: $8.00.

MANY articles in this book on planning have appeared from time to time in the various journals, but this is the first time an entire book has been devoted to the subject. It records the findings of a large committee consisting of radiologists, manufacturers, health officers, members of the American Medical Association and members of the American Institute of Architects. There is quite an amount of repetition in the book owing to the fact that different individuals have written on various phases of the subject. A most interesting section deals with the amount and type of work done in various institutions, with the numbers of skilled personnel engaged in this work. It is stated that it is necessary to spend £700 for each daily patient to equip thoroughly and to furnish a department capable of dealing with every class of X-ray work. Good ventilation and natural light should be available and bright colours should be used for the walls. A very important chapter is devoted to "Don'ts". There is extensive detail given on protection of personnel in both diagnostic and therapeutic departments. Methods of storing and filing films in special compartments are suggested. Floor plans for examination rooms, dark rooms and dressing rooms have been carefully prepared and should prove of value. The book is a most interesting one and should be of special value to architects engaged in hospital construction.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Clinical Endocrinology", by Karl E. Paschkis, M.D., Abraham E. Rakoff, M.D., and Abraham Cantarow, M.D.; 1954. New York: Paul B. Hoeber, Incorporated. 9¼" × 6¼", pp. 842, with 253 illustrations, five in colour. Price: $16.00.

This book has been written with the idea that clinical endocrine disorders can be understood fully only when seen as problems in pathological physiology.

"Cold Injury: Transactions of the Second Conference, November 20 and 21, 1952, New York", edited by M. Irené Ferrer; 1954. New York: Josiah Macy Junior Foundation. 9" × 6¼", pp. 242, with 43 illustrations, two in colour. Price: $4.00.

Deals with epidemiology of cold injury, resistance to cold, pathophysiology of cold injuries and suggested areas for future discussion and research.

"Modern Medical Monographs: An Rh-Hr Syllabus: The Types and Their Applications", by Alexander S. Wiener, M.D., F.A.C.P., F.C.A.P.; 1954. New York: Grune and Stratton. 9" × 5¾", pp. 94, with nine illustrations. Price: $3.75.

This book presents the serology and genetics of the Rh-Hr types and also deals with Rh antibody tests. Practical details of related subjects are included.

"Headache: Diagnosis and Treatment", by Robert E. Ryan, B.S., M.D., M.S. (in Otolaryngology), F.A.C.S.; 1954. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited 9" × 6", pp. 338, with three illustrations. Price: £3 8s. 3d.

The author discusses "as many different forms of headache and head pain and as many as possible different forms of pathologic conditions which produce headache".

"Entomology (Medical and Veterinary): Including Insecticides and Insect and Rat Control", by D. N. Roy, M.D., D.T.M., D.Sc., and A. W. A. Brown, M.B.E., Ph.D.; Second Edition; 1954. Calcutta: Excelsior Press. 10" × 7½", pp. 422, with 205 illustrations. Price: Rs. 30.

Designed to assist the medical entomologist who combines the functions of an entomologist, a biologist and a parasitologist.

"Pediatric Clinics of North America: Symposium on Cardiovascular Diseases"; 1954. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9" × 6", pp. 288, with 96 illustrations. Price: £6 per year.

This is the first issue of a new journal.

"Medical Terms: Their Origin and Construction", by Ffrangcon Roberts, M.A., M.D., F.F.R.; 1954. London: William Heinemann (Medical Books), Limited. 7½" × 5", pp. 96. Price: 6s.

Intended to help the reader to deduce the derivation of medical terms.

"Helping Troubled People: Personal Counselling for Ministers, Doctors and Laymen", by W. L. Carrington, M.D.; 1954. London: The Epworth Press. 7½" × 5", pp. 56. Price: 4s.

The book is an attempt to put into brief and simple terms some of the principles and practice of personal counselling in its modern form.

"Spot Diagnosis: With Notes on Therapy", compiled by the editors of *Medicine Illustrated*; 1954. London: Harvey and Blythe, Limited. Volume I. 9" × 6", pp. 128, with 110 illustrations. Price: 7s. 6d.

The book contains photographs showing the characteristics of various diseases with clues to the diagnosis.

The Medical Journal of Australia

SATURDAY, MAY 22, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

VITAMIN C REQUIREMENTS OF HUMAN ADULTS.

SINCE the discovery and subsequent synthesis of ascorbic acid there has been a great deal of discussion all over the world on the amount required per day by human beings to prevent the onset of scurvy and to provide for all needs. Estimates vary from 10 milligrammes per day to over 100 milligrammes. The League of Nations Technical Commission on Nutrition in 1938 estimated that 30 milligrammes were sufficient. This figure has been accepted by most British and other European authorities. In 1943 the National Research Council Committee on Food and Nutrition of the United States of America recommended an allowance of 75 milligrammes and have maintained this figure in each report published since then. For neither of these recommendations was there adequate experimental evidence. A point in favour of the lower amount, 30 milligrammes, is the fact that this was approximately the amount consumed by most inhabitants of Great Britain during the last war, and scorbutic symptoms were rare in the population, if they occurred at all. The larger amount, 75 milligrammes, is very difficult to obtain by many people without the consumption of oranges and other fruit of high ascorbic acid content. In order to obtain additional information of a more accurate nature than was available, the British Medical Research Council set up a committee in 1944 whose plan was to induce scurvy by a diet deficient in vitamin *C* and to establish the minimum dose of the vitamin that cures scurvy. A subsidiary aim was to study the clinical signs and symptoms of scurvy and to correlate them with laboratory findings.

In May, 1953, the Nutrition Society of Britain held a "Lind Bicentenary Symposium on Scurvy" in honour of James Lind whose *Treatise on the Scurvy* was published in 1753. The addresses given at that symposium are now published in the *Proceedings of the Nutrition Society* as a special number.[1] Among those making up a valuable collection of papers are two which have special reference to human requirements: "The Sheffield Experiment on the Vitamin C Requirement of Human Adults", by H. A. Krebs, and "Ascorbic Acid Deficiency in Experimental and Surgical Subjects", by J. H. Crandon, S. Mikal and B. R. Landeau, of Boston, United States of America. Professor Krebs's paper gives a long summary of the main aspects of the trial conducted by the Vitamin *C* Subcommittee of the Medical Research Council, the full report of which was published by Her Majesty's Stationery Office in 1953. Nineteen men and one woman, aged twenty-one to thirty-four years, volunteered for the experiment. They lived a normal life without strenuous physical work. Their basal diet was designed to be as low as possible in vitamin *C* content, but complete in every other respect including acceptability. On an average not more than one milligramme of ascorbic acid per day was obtained from the diet. For a preliminary period of about six weeks all the subjects were given a full diet with 70 milligrammes per day of ascorbic acid. At the end of this period all the subjects were given the basal deficient diet and divided into three groups; ten had no supplements, seven had ten milligrammes of ascorbic acid and three had 70 milligrammes per day. All the subjects received tablets with or without ascorbic acid; none knew what they were getting, nor did the physicians responsible for the clinical investigations. The clinical examinations, by inspection and physical methods, revealed no definite changes during the first seventeen weeks of deprivation. The first changes which retrospectively were recognized as significant were enlargement and keratosis of the hair follicles, particularly on the outer aspect of the upper arm. After twenty-six weeks all the ten deprived subjects had developed these changes. In all but one the enlarged hair follicles eventually became hæmorrhagic. Five of the ten subjects had mild acne at the start; these showed a marked exacerbation of the acne, and the papules increased in size and became bright red. Other changes generally noted during the period of deprivation were in the gums; tiny hæmorrhages in the tips of the interdental papillæ were first noted after twenty-six weeks of deprivation. Another striking observation, in agreement with the old accounts of scurvy, was made after thirty weeks in six subjects; scars of wounds made earlier in the test, which had healed normally, became red and livid. Marked cardiac changes were seen in two of the deprived subjects with a picture of an acute cardiac emergency; they were immediately given a large dose of ascorbic acid and recovered rapidly. It may be relevant to this to note that the older records of scurvy contain many references to sudden death, especially after exertion. Neither hyperkeratosis nor congestion of the hair follicles is a specific sign, and they may occur in persons "saturated" with vitamin *C*. The gum lesions always appeared after the skin lesions, and thus might be a useful diagnostic pointer when gum lesions of unknown origin are present. Many

[1] *Proc. Nutrition Soc.*, 1953, Volume XII, Number 3.

signs listed as scorbutic in the classical descriptions of the disease were not observed, leading to the belief that classical scurvy was often a multiple deficiency. In the seven volunteers receiving ten milligrammes of ascorbic acid daily no abnormalities were noted during one hundred and sixty days of the test. Three received the ten milligrammes for another two hundred and sixty-four days. No abnormalities were recorded; so that ten milligrammes daily gave complete protection from clinical scurvy for up to four hundred and twenty-four days. Six of the deprived volunteers with unequivocal signs of scurvy were given ten milligrammes of ascorbic acid daily. All signs disappeared within ten to fourteen weeks. In the subjects receiving no ascorbic acid and in those receiving ten milligrammes daily the plasma content of ascorbic acid fell to almost nothing in about four weeks and remained at these low levels. The ascorbic acid content of the white cells fell to below two milligrammes per hundred grammes of cells in the totally deprived subjects, but did not fall below two milligrammes in those receiving ten milligrammes per day. It is believed from these experiments that a concentration below two milligrammes per 100 grammes in the white cells, especially when confirmed by repeated examinations, indicates severe depletion and would support a diagnosis of scurvy. The volunteers receiving 70 milligrammes of ascorbic acid per day remained normal throughout the test. The main facts relevant to the assessment of requirements are as follows: (i) A supplement of ten milligrammes cured clinical scurvy in all six subjects examined. (ii) A supplement of ten milligrammes protected seven volunteers throughout the period of observation, up to four hundred and twenty-four days. (iii) When a ten-milligramme supplement was withdrawn from three volunteers after one hundred and sixty days and was followed by a period of one hundred and ninety-five days when the intake varied between three and four milligrammes daily, no definite clinical signs developed. These observations suggest that the "minimum protective dose" of ascorbic acid is in the region of, and probably somewhat below, ten milligrammes per day. To satisfy certain ill-defined additional needs, such as greater activity, a trebling of this dose should be sufficient, and 30 milligrammes of ascorbic acid per day may be taken as a reasonable requirement so long as there is no evidence to support the view that a larger intake is beneficial.

J. H. Crandon's experiment with one normal subject deprived of ascorbic acid gave essentially similar results to those in the Sheffield experiments. Crandon and his colleagues studied 561 selected surgical patients at the Boston City Hospital, using determinations of plasma and white cell ascorbic acid content as indications of intake. They found traces of ascorbic acid in the plasma and white cells of patients who were frankly scorbutic, and concluded that clinical scurvy is a result not of ascorbic acid deficiency, but of ascorbic acid deficiency *plus* tissue stress, as suggested in another form by Lind two hundred years ago. (See THE MEDICAL JOURNAL OF AUSTRALIA, September 12, 1953, page 423.) In surgical cases they found a close association of low ascorbic acid content of the blood and high wound complication rate. No increased incidence of wound complications was observed among those patients having a deficient plasma content but a buffy-coat ascorbic acid level consistently above eight milligrammes per hundred grammes, provided there existed no wound infection or other increased local tissue stress. A weakness in the work is the absence of any information about the ascorbic acid intake. It is probable that a higher ascorbic acid intake is necessary when tissue stress is present, but there is no information as yet on how much more is needed above minimum requirements.

In another paper in the same journal R. M. Kark discusses the relation of ascorbic acid intake to exposure to extreme cold. He states that the evidence obtained from work in the far north of Canada failed to show that, so far as man is concerned, the stress of cold significantly increases ascorbic acid requirements. Kark seems to have depended almost wholly on blood ascorbic acid estimations in assessing the ascorbic acid intake, and the only place where quantity of intake is stated is in this sentence: "Calculation of metabolic balances for ascorbic acid showed the men to be in balance with a daily intake of from 30 to 40 mgm. of vitamin C." The evidence available then at the present time is that 30 milligrammes of ascorbic acid per day should fill all requirements except possibly in cases of severe tissue stress.

Current Comment.

ISOLATION OF THE INTRINSIC FACTOR OF CASTLE.

IN 1929 W. B. Castle demonstrated the presence in the gastric juice of normal persons of what he called the intrinsic factor, and his name has remained associated with this term. The intrinsic factor, in conjunction with a dietary factor called by Castle the extrinsic factor, was found to have a curative effect when given by mouth to patients suffering from pernicious anæmia. The intrinsic principle appeared to be absent from the gastric juice of a patient suffering from pernicious anæmia. Later it was found that the intrinsic factor could be obtained from the stomach tissue of certain animals. The site of its formation in human beings was shown to be the fundus of the stomach. A fairly simple theory was formulated of the way in which these factors acted in relation to pernicious anæmia. It is set out in the following manner by C. H. Best and N. B. Taylor in their text-book "The Physiological Basis of Medical Practice". In health, the essential anti-anæmic principle is derived from food through the action of the intrinsic (gastric) factor upon an extrinsic factor contained in the diet. The anti-anæmic principle so formed is stored in the liver and possibly other organs, to be drawn upon for maintenance of normal activity of the erythropoietic tissue (bone marrow). Pernicious anæmia follows if the essential enzyme is absent from the gastric juice. The anti-anæmic principle can therefore be given pre-formed, as in liver or liver extract; or gastric tissue in combination with a well-balanced diet can be given, and from this the patient manufactures his own supplies. This theory has, in broad terms, been supported by clinical experience.

For a long time, the nature of the intrinsic and extrinsic factors was obscure. Then, in 1948, groups of workers, both in the United States and in England, independently isolated the cobalt-containing substance to which the name vitamin B_{12}, or cobalamin, was given. In a short summary of current knowledge of vitamin B_{12} published in this journal last year, Sidney D. Rubbo[1] points out that vitamin B_{12} is equivalent to Castle's extrinsic factor in that, when

[1] M. J. AUSTRALIA, March 7, 1953.

administered orally with a source of intrinsic factor, it stimulates a hæmatopoietic response in the pernicious anæmia subject. Pernicious anæmia responds satisfactorily to vitamin B_{12} when given intramuscularly, but not when given alone by mouth. The desired hæmatopoietic response does, however, follow the combined oral administration of vitamin B_{12} with intrinsic factor in a majority of cases of pernicious anæmia. It appears that the effective absorption of vitamin B_{12} from the alimentary tract depends upon the presence of intrinsic factor, with which it is "bound". Vitamin B_{12} is, then, probably the extrinsic factor of Castle, or at least an extrinsic factor.

The intrinsic factor has been even more elusive, but it seems likely that it has now been isolated. As with vitamin B_{12}, parallel work on the intrinsic factor has been going on in both the United States and in England. Last year, A. L. Latner and C. C. Ungley, with a group of collaborators,[1] reported a method of preparing intrinsic factor concentrates from human gastric juice. The more active of the material obtained was shown to contain either a mucoprotein or a mucopolysaccharide. The methods employed involved ultrafiltration and freeze-drying followed by preparative electrophoresis on filter paper. The concentrates were tested by the hæmatological responses produced in patients suffering from untreated pernicious anæmia after oral administration of the material, together with vitamin B_{12}. Latner, writing in conjunction with R. J. Merrills and L. C. D. P. Raine, now reports[2] isolation of the intrinsic factor "in a satisfactorily pure state". Subsequently to the experiments already mentioned, the electrophoresis method was applied to a concentrate derived from hog gastric mucosa. The buffer electrolytes in each fraction were removed by ultrafiltration and the solutions freeze-dried. The highly active solid material so obtained proved to be mucoprotein in nature. It was tested for intrinsic factor activity by determining its effect on the fæcal excretion of radioactive vitamin B_{12} administered orally. A diminished excretion in the fæces was taken as evidence of intrinsic factor activity. Latner, Merrills and Raine go on to state that, making use of data obtained from the study of the variation in the solubility of the electrophoresis material with varying pH and in certain salt solutions, they have now succeeded in isolating the active mucoprotein from the crude extract without resort to any form of preparative electrophoresis. Chemical analysis has demonstrated a close similarity between the new material and the active factors of fractions obtained previously by electrophoresis. Both methods have yielded fractions highly effective in diminishing the fæcal excretion of radioactive vitamin B_{12} administered orally. Examination by paper-strip electrophoresis has indicated that the most recently obtained material and the best electrophoresis fractions are essentially homogeneous. Examination of the most recently obtained material in the ultracentrifuge has shown it to contain a small amount of protein of high molecular weight which undergoes sedimentation rapidly; the remaining material, representing 95% of the original, appears homogeneous and has a molecular weight below 20,000. These investigators have thus obtained by different procedures active fractions resembling one another very closely. The similarity relates to chemical analysis, behaviour during electrophoresis and biological activity. These facts, taken together with ultracentrifuge data, are regarded by Latner, Merrills and Raine as evidence of chemical purity of the material isolated.

The main clinical importance of this work of isolating intrinsic and extrinsic factors probably lies in the simplification of treatment. A number of reports have appeared in both the United States and England describing the treatment of patients suffering from pernicious anæmia by oral administration of a combination of vitamin B_{12} and various forms of intrinsic factor concentrate. In particular, we may mention papers by G. B. J. Glass and L. J. Boyd[3] and by C. P. Lowther, W. D. Alexander and E. B. Hendry.[4] Glass and Boyd treated 20 patients suffering from pernicious anæmia in various stages—in full relapse, in the initial period of "full-blown" disease and in remission. The intrinsic factor in all cases came from hog's stomach, but was prepared in various ways. Lowther, Alexander and Hendry's subjects were 20 patients suffering from pernicious anæmia, in remission and satisfactorily controlled, who were transferred to treatment with "Bifacton", a proprietary combination of vitamin B_{12} and intrinsic factor, used also by Glass and Hoad for some of their patients. In both series, so far as can be judged from the limited period of observation, the results have been satisfactory. By these means, oral treatment of persons suffering from pernicious anæmia would seem to be a practical possibility. This has obvious advantages. However, one drawback of a very down-to-earth nature needs to be mentioned. Lowther, Alexander and Hendry at the conclusion of their report refer to previous experience of the type of patient who cannot be trusted to continue oral therapy unless under constant supervision. The patient who has to receive repeated injections from his doctor is under complete and regular control, and the progress of his condition can be assessed from time to time as his medical adviser thinks necessary. Supervision of this kind is less readily maintained when oral therapy is used, and it is suggested that the advantage in this direction occasioned by the repeated injections is one not lightly to be abandoned.

[1] *Brit. M. J.*, February 28, 1953.
[2] *Lancet*, March 6, 1954.
[3] *Blood*, October, 1953.
[4] *Lancet*, March 6, 1954.

EMERGENCY RATIONS.

IN times of emergency such as a shipwreck or when an aeroplane makes a forced landing in the sea or desert a man still needs food and water. Under these conditions the rations must be designed to be as compact and light as possible. At rest, in an equable environment, a healthy man without water loses *per diem* about 900 millilitres of water through the lungs and skin and about 400 millilitres in the urine. He generates about 200 millilitres through his own metabolism. His requirements from outside sources are therefore just over a litre a day. He must have also enough food every day to provide him with 1500 to 2000 Calories. Ideally emergency rations should supply these requirements, but in practice it may be impossible to carry enough even for a few days and some deterioration is inevitable. An inadequate supply of water is the most dangerous. Without food life is maintained by the energy derived from the metabolism of the tissues of the body, so there is loss of body weight, but over a period of two weeks harmful effects are relatively slight. G. R. Hervey and R. A. McCance[1] in a symposium at a meeting of the Nutrition Society in London on the provisioning of expeditions in the field discussed the composition of concentrated emergency rations which would be relatively adequate to prevent undue deterioration. When there is insufficient intake of water the urine is maximally concentrated, and its volume varies with the output of solids. The solids are mainly the end-products of protein metabolism and salts. Protein breakdown can be reduced by generous intake of carbohydrates and fat, but it was not appreciated until recently how small an amount of carbohydrate is required to produce the effect. On six male subjects an experiment was done in which water only or water and carbohydrate were given. On the third day the figures were: water given 350 millilitres, protein katabolized 78 grammes, urine volume 680 millilitres, water deficit 980 millilitres. When 250 millilitres of water and 96·5 grammes of carbohydrate were given the protein katabolized was 43 grammes, the urine volume was 360 millilitres and the water deficit 750 millilitres, so that with the carbohydrate and 100 millilitres less water 230 millilitres more water was retained in the body. The giving of salt to dehydrated men has been shown to increase their urine volume. Rations therefore should contain as little salt as possible.

Three rations are suggested. The first is termed the desirable ration which should prevent deterioration of a healthy man at rest. This consists of water 1400 grammes,

[1] *Proc. Nutrition Soc.*, Volume 13, No. 1, 1954.

signs listed as scorbutic in the classical descriptions of the disease were not observed, leading to the belief that classical scurvy was often a multiple deficiency. In the seven volunteers receiving ten milligrammes of ascorbic acid daily no abnormalities were noted during one hundred and sixty days of the test. Three received the ten milligrammes for another two hundred and sixty-four days. No abnormalities were recorded; so that ten milligrammes daily gave complete protection from clinical scurvy for up to four hundred and twenty-four days. Six of the deprived volunteers with unequivocal signs of scurvy were given ten milligrammes of ascorbic acid daily. All signs disappeared within ten to fourteen weeks. In the subjects receiving no ascorbic acid and in those receiving ten milligrammes daily the plasma content of ascorbic acid fell to almost nothing in about four weeks and remained at these low levels. The ascorbic acid content of the white cells fell to below two milligrammes per hundred grammes of cells in the totally deprived subjects, but did not fall below two milligrammes in those receiving ten milligrammes per day. It is believed from these experiments that a concentration below two milligrammes per 100 grammes in the white cells, especially when confirmed by repeated examinations, indicates severe depletion and would support a diagnosis of scurvy. The volunteers receiving 70 milligrammes of ascorbic acid per day remained normal throughout the test. The main facts relevant to the assessment of requirements are as follows: (i) A supplement of ten milligrammes cured clinical scurvy in all six subjects examined. (ii) A supplement of ten milligrammes protected seven volunteers throughout the period of observation, up to four hundred and twenty-four days. (iii) When a ten-milligramme supplement was withdrawn from three volunteers after one hundred and sixty days and was followed by a period of one hundred and ninety-five days when the intake varied between three and four milligrammes daily, no definite clinical signs developed. These observations suggest that the "minimum protective dose" of ascorbic acid is in the region of, and probably somewhat below, ten milligrammes per day. To satisfy certain ill-defined additional needs, such as greater activity, a trebling of this dose should be sufficient, and 30 milligrammes of ascorbic acid per day may be taken as a reasonable requirement so long as there is no evidence to support the view that a larger intake is beneficial.

J. H. Crandon's experiment with one normal subject deprived of ascorbic acid gave essentially similar results to those in the Sheffield experiments. Crandon and his colleagues studied 561 selected surgical patients at the Boston City Hospital, using determinations of plasma and white cell ascorbic acid content as indications of intake. They found traces of ascorbic acid in the plasma and white cells of patients who were frankly scorbutic, and concluded that clinical scurvy is a result not of ascorbic acid deficiency, but of ascorbic acid deficiency *plus* tissue stress, as suggested in another form by Lind two hundred years ago. (See THE MEDICAL JOURNAL OF AUSTRALIA, September 12, 1953, page 423.) In surgical cases they found a close association of low ascorbic acid content of the blood and high wound complication rate. No increased incidence of wound complications was observed among those patients having a deficient plasma content but a buffy-coat ascorbic acid level consistently above eight milligrammes per hundred grammes, provided there existed no wound infection or other increased local tissue stress. A weakness in the work is the absence of any information about the ascorbic acid intake. It is probable that a higher ascorbic acid intake is necessary when tissue stress is present, but there is no information as yet on how much more is needed above minimum requirements.

In another paper in the same journal R. M. Kark discusses the relation of ascorbic acid intake to exposure to extreme cold. He states that the evidence obtained from work in the far north of Canada failed to show that, so far as man is concerned, the stress of cold significantly increases ascorbic acid requirements. Kark seems to have depended almost wholly on blood ascorbic acid estimations in assessing the ascorbic acid intake, and the only place where quantity of intake is stated is in this sentence: "Calculation of metabolic balances for ascorbic acid showed the men to be in balance with a daily intake of from 30 to 40 mgm. of vitamin C." The evidence available then at the present time is that 30 milligrammes of ascorbic acid per day should fill all requirements except possibly in cases of severe tissue stress.

Current Comment.

ISOLATION OF THE INTRINSIC FACTOR OF CASTLE.

IN 1929 W. B. Castle demonstrated the presence in the gastric juice of normal persons of what he called the intrinsic factor, and his name has remained associated with this term. The intrinsic factor, in conjunction with a dietary factor called by Castle the extrinsic factor, was found to have a curative effect when given by mouth to patients suffering from pernicious anæmia. The intrinsic principle appeared to be absent from the gastric juice of a patient suffering from pernicious anæmia. Later it was found that the intrinsic factor could be obtained from the stomach tissue of certain animals. The site of its formation in human beings was shown to be the fundus of the stomach. A fairly simple theory was formulated of the way in which these factors acted in relation to pernicious anæmia. It is set out in the following manner by C. H. Best and N. B. Taylor in their text-book "The Physiological Basis of Medical Practice". In health, the essential anti-anæmic principle is derived from food through the action of the intrinsic (gastric) factor upon an extrinsic factor contained in the diet. The anti-anæmic principle so formed is stored in the liver and possibly other organs, to be drawn upon for maintenance of normal activity of the erythropoietic tissue (bone marrow). Pernicious anæmia follows if the essential enzyme is absent from the gastric juice. The anti-anæmic principle can therefore be given pre-formed, as in liver or liver extract; or gastric tissue in combination with a well-balanced diet can be given, and from this the patient manufactures his own supplies. This theory has, in broad terms, been supported by clinical experience.

For a long time, the nature of the intrinsic and extrinsic factors was obscure. Then, in 1948, groups of workers, both in the United States and in England, independently isolated the cobalt-containing substance to which the name vitamin B_{12}, or cobalamin, was given. In a short summary of current knowledge of vitamin B_{12} published in this journal last year, Sidney D. Rubbo[1] points out that vitamin B_{12} is equivalent to Castle's extrinsic factor in that, when

[1] M. J. AUSTRALIA, March 7, 1953.

administered orally with a source of intrinsic factor, it stimulates a hæmatopoietic response in the pernicious anæmia subject. Pernicious anæmia responds satisfactorily to vitamin B_{12} when given intramuscularly, but not when given alone by mouth. The desired hæmatopoietic response does, however, follow the combined oral administration of vitamin B_{12} with intrinsic factor in a majority of cases of pernicious anæmia. It appears that the effective absorption of vitamin B_{12} from the alimentary tract depends upon the presence of intrinsic factor, with which it is "bound". Vitamin B_{12} is, then, probably the extrinsic factor of Castle, or at least an extrinsic factor.

The intrinsic factor has been even more elusive, but it seems likely that it has now been isolated. As with vitamin B_{12}, parallel work on the intrinsic factor has been going on in both the United States and in England. Last year, A. L. Latner and C. C. Ungley, with a group of collaborators,[1] reported a method of preparing intrinsic factor concentrates from human gastric juice. The more active of the material obtained was shown to contain either a mucoprotein or a mucopolysaccharide. The methods employed involved ultrafiltration and freeze-drying followed by preparative electrophoresis on filter paper. The concentrates were tested by the hæmatological responses produced in patients suffering from untreated pernicious anæmia after oral administration of the material, together with vitamin B_{12}. Latner, writing in conjunction with R. J. Merrills and L. C. D. P. Raine, now reports[2] isolation of the intrinsic factor "in a satisfactorily pure state". Subsequently to the experiments already mentioned, the electrophoresis method was applied to a concentrate derived from hog gastric mucosa. The buffer electrolytes in each fraction were removed by ultrafiltration and the solutions freeze-dried. The highly active solid material so obtained proved to be mucoprotein in nature. It was tested for intrinsic factor activity by determining its effect on the fæcal excretion of radioactive vitamin B_{12} administered orally. A diminished excretion in the fæces was taken as evidence of intrinsic factor activity. Latner, Merrills and Raine go on to state that, making use of data obtained from the study of the variation in the solubility of the electrophoresis material with varying pH and in certain salt solutions, they have now succeeded in isolating the active mucoprotein from the crude extract without resort to any form of preparative electrophoresis. Chemical analysis has demonstrated a close similarity between the new material and the active factors of fractions obtained previously by electrophoresis. Both methods have yielded fractions highly effective in diminishing the fæcal excretion of radioactive vitamin B_{12} administered orally. Examination by paper-strip electrophoresis has indicated that the most recently obtained material and the best electrophoresis fractions are essentially homogeneous. Examination of the most recently obtained material in the ultracentrifuge has shown it to contain a small amount of protein of high molecular weight which undergoes sedimentation rapidly; the remaining material, representing 95% of the original, appears homogeneous and has a molecular weight below 20,000. These investigators have thus obtained by different procedures active fractions resembling one another very closely. The similarity relates to chemical analysis, behaviour during electrophoresis and biological activity. These facts, taken together with ultracentrifuge data, are regarded by Latner, Merrills and Raine as evidence of chemical purity of the material isolated.

The main clinical importance of this work of isolating extrinsic and extrinsic factors probably lies in the simplification of treatment. A number of reports have appeared in both the United States and England describing the treatment of patients suffering from pernicious anæmia by oral administration of a combination of vitamin B_{12} and various forms of intrinsic factor concentrate. In particular, we may mention papers by G. B. J. Glass and L. J. Boyd[3] and by C. P. Lowther, W. D. Alexander and E. B. Hendry.[4] Glass and Boyd treated 20 patients suffering from pernicious anæmia in various stages—in full relapse, in the initial period of "full-blown" disease and in remission. The intrinsic factor in all cases came from hog's stomach, but was prepared in various ways. Lowther, Alexander and Hendry's subjects were 20 patients suffering from pernicious anæmia, in remission and satisfactorily controlled, who were transferred to treatment with "Bifacton", a proprietary combination of vitamin B_{12} and intrinsic factor, used also by Glass and Hoad for some of their patients. In both series, so far as can be judged from the limited period of observation, the results have been satisfactory. By these means, oral treatment of persons suffering from pernicious anæmia would seem to be a practical possibility. This has obvious advantages. However, one drawback of a very down-to-earth nature needs to be mentioned. Lowther, Alexander and Hendry at the conclusion of their report refer to previous experience of the type of patient who cannot be trusted to continue oral therapy unless under constant supervision. The patient who has to receive repeated injections from his doctor is under complete and regular control, and the progress of his condition can be assessed from time to time as his medical adviser thinks necessary. Supervision of this kind is less readily maintained when oral therapy is used, and it is suggested that the advantage in this direction occasioned by the repeated injections is one not lightly to be abandoned.

[1] *Brit. M. J.*, February 28, 1953.
[2] *Lancet*, March 6, 1954.
[3] *Blood*, October, 1953.
[4] *Lancet*, March 6, 1954.

EMERGENCY RATIONS.

In times of emergency such as a shipwreck or when an aeroplane makes a forced landing in the sea or desert a man still needs food and water. Under these conditions the rations must be designed to be as compact and light as possible. At rest, in an equable environment, a healthy man without water loses *per diem* about 900 millilitres of water through the lungs and skin and about 400 millilitres in the urine. He generates about 200 millilitres through his own metabolism. His requirements from outside sources are therefore just over a litre a day. He must have also enough food every day to provide him with 1500 to 2000 Calories. Ideally emergency rations should supply these requirements, but in practice it may be impossible to carry enough even for a few days and some deterioration is inevitable. An inadequate supply of water is the most dangerous. Without food life is maintained by the energy derived from the metabolism of the tissues of the body, so there is loss of body weight, but over a period of two weeks harmful effects are relatively slight. G. R. Hervey and R. A. McCance[1] in a symposium at a meeting of the Nutrition Society in London on the provisioning of expeditions in the field discussed the composition of concentrated emergency rations which would be relatively adequate to prevent undue deterioration. When there is insufficient intake of water the urine is maximally concentrated, and its volume varies with the output of solids. The solids are mainly the end-products of protein metabolism and salts. Protein breakdown can be reduced by generous intake of carbohydrates and fat, but it was not appreciated until recently how small an amount of carbohydrate is required to produce the effect. On six male subjects an experiment was done in which water only or water and carbohydrate were given. On the third day the figures were: water given 350 millilitres, protein katabolized 78 grammes, urine volume 680 millilitres, water deficit 980 millilitres. When 250 millilitres of water and 96·5 grammes of carbohydrate were given the protein katabolized was 43 grammes, the urine volume was 360 millilitres and the water deficit 750 millilitres, so that with the carbohydrate and 100 millilitres less water 230 millilitres more water was retained in the body. The giving of salt to dehydrated men has been shown to increase their urine volume. Rations therefore should contain as little salt as possible.

Three rations are suggested. The first is termed the desirable ration which should prevent deterioration of a healthy man at rest. This consists of water 1400 grammes,

[1] *Proc. Nutrition Soc.*, Volume 13, No. 1, 1954.

boiled sweets 100 grammes, toffee (30% fat) 100 grammes, biscuits (about 20% fat) 100 grammes, sweetened condensed milk 100 grammes, with a total net weight of 1800 grammes and Calorie value of 1750. The third or minimum ration, on which a man would lose between 1% and 2% of his body weight a day, but remain fairly well for one week and survive two or more weeks, consisted of water 500 grammes and boiled sweets 100 grammes. The compromise ration was the same as the desirable ration with only 800 grammes of water and no biscuits. This should keep a man in reasonable efficiency for three weeks or more. Various changes could be made in these rations, but the substances chosen are stable and palatable and easily obtained. As will be seen, the water accounts for by far the greater part of the weight. Environment is important and may alter the requirements. In a small boat or on a raft the motion may cause seasickness and greatly increase the loss of water, so hyoscine should be included in raft equipment and taken by all. Sitting in an open boat in the tropics a man may lose up to five litres of water in twenty-four hours by sweating, so shade should be arranged and exertion avoided where possible. Wetting the clothes with sea water during the day is helpful.

ENDOMETRIAL CHANGES AND CANCER.

VARIOUS opinions are held on the question of what are the earliest endometrial changes that justify a diagnosis of endometrial cancer. According to R. W. Te Linde, H. W. Jones and G. A. Galvin,[1] the accumulated data do not justify an entirely fixed opinion on the part of anyone, but the ultimate correct solution to this question is of considerable moment. It is important from the point of view not only of diagnosis and treatment of the patient, but of reporting and comparing salvage statistics. Te Linde, Jones and Galvin refer to the great difference of opinion among pathologists in interpreting the features of sections of biopsy material, the lesions found being described as "atypical hyperplasia", "proliferative hyperplasia", "focal hyperplasia" and "adenomatous hyperplasia". However, it has become recognized that there is some type of relationship between hyperplasia and corporeal cancer, especially hyperplasia after the menopause. Te Linde, Jones and Galvin offer the following summary of the present-day conception of focal hyperplasia, adenomatous hyperplasia and endometrial carcinoma *in situ*. Focal hyperplasia is described as having a characteristic infolding of the glandular epithelium and appears to bear no time relation to the development of cancer. Adenomatous hyperplasia shows an outpouching of bud-like glandular projections into the supporting stroma; although this hyperplasia sometimes regresses, it is more commonly found to be a precursor of endometrial cancer. Carcinoma *in situ* of the endometrium is characterized by foci of glands formed of large eosinophilic cells with pale nuclei; this condition does not regress, and overt cancer has been found to follow in from one to eleven years. Te Linde, Jones and Galvin report a detailed study of 35 patients, comparing the histological findings from examination of earlier curettage material with those of the ultimately removed uterus. In the first group of 13 cases, the findings from curettage were open to question, and immediate hysterectomy was performed. In 11 of these 13 cases, study of the uterus after hysterectomy showed undoubted endometrial cancer, with myometrial invasion in five cases. The second group comprised 14 cases in which the interpretation of the appearance of curettage material was questionable, but treatment was not carried out immediately; operation became necessary at intervals of ten months to three years later on account of bleeding, and frank carcinoma was found. The data presented in relation to this group suggest that often endometrial carcinoma may be preceded by similar "hyperplastic" lesions for several years. The third group was made up of eight cases of adenocarcinoma of the endometrium studied in retrospect; in these, material from previous curettage obtained from three to thirty-four years before was available for study. Observations on this group indicate that endometrium affected by adenocarcinoma is preceded sometimes by endometrium going through a normal cycle, non-secretory endometrium or endometrium with glandular cystic hyperplasia. Te Linde, Jones and Galvin think it possible that lesions described as atypical hyperplasia, proliferative hyperplasia and adenomatous hyperplasia may bear the same relation to advanced endometrial cancer as carcinoma *in situ* bears to invasive cervical cancer. It appears that some of these lesions, like epidermoid cancer *in situ*, may precede actual cancer for many years or may coexist with it. There is at least the suggestion from this study that the stimulus which ultimately brings about the development of invasive endometrial cancer may in some cases be at work for many years.

[1] *Am. J. Obstet. & Gynec.*, November, 1953.

THE SYNDROME OF COUGH SYNCOPE.

MEDICAL LITERATURE is scattered with numbers of named syndromes whose ætiology and nature are in some ways obscure. One of these has been recently redescribed by Andrew Kerr and Vincent J. Derbes, and the name they use, "cough syncope", is perhaps as illuminating as any.[1] A bibliography of 44 items indicates how many people have been interested in this condition, which appears to be not so much important as alarming. A perusal of the titles of articles on the subject shows how widely different some of these names are, and the authors append a footnote in which they have collected 42 names all applied to what we may agree is the same condition. The fact that some of these titles must be inaccurate is interesting, and shows that the naming of a clinical syndrome or disease is surely more difficult than the naming of a child. Indeed the history of medicine illustrates the danger of begging the question of ætiology in choosing a name. Cough syncope is a name purely descriptive, and correct in that it tags a state in which sudden loss of consciousness occurs after a cough or fit of coughing. Some of the authorities who have described this condition use the word vertigo, which seems quite without justification, as vertigo is not necessarily a characteristic feature of the syndrome. To call it "laryngeal epilepsy" is still more misleading, as epilepsy as a term in itself requires some description. However, the authors have turned from the usual dignified medical style of description and have used the technique of the so-called "comic strip" to make clear what it is that they are describing. Their cartoonist depicts a thick-set middle-aged man, "balding" as American journalists say, standing with a foot on the bar rail, drink in hand. He is shown coughing, and next is seen fallen on the floor, though still holding his cigar, and obviously not in full possession of his faculties. The artist leaves one in doubt whether the patient is dizzy or unconscious, but in the final picture there is no doubt; he is fully conscious, but unaware of his spectacular display as he finishes his uncompleted sentence to tell his friends that his cough, which he has had for years, never bothers him. It is not suggested that the cartoon technique should invade clinical medicine, but perhaps there are times when description could be simplified by its use.

Coming to the syndrome itself, it cannot be uncommon, as so many authorities have described it and speculated on its nature. The present authors have collected 25 typical cases on which they base their account. It is interesting that they describe their patients as "of an outgoing personality, who frequently over indulge in tobacco, alcohol and food". Their cases are confined to the male. The most striking point in this condition is stressed by them, the sudden occurrence of syncope, and the rapid recovery of consciousness with a minimum of sequelæ. The diagnosis offers no difficulty as a rule, and Kerr and

[1] *Ann. Int. Med.*, December, 1953.

Derbes agree that only laryngeal crises of tabes can be confused with it. Epilepsy, as previously remarked, has come into the diagnostic reckoning also, and it is admitted that there are similarities to the cataplectic attacks of the narcoleptic state. It is possible that there may indeed be more than one or two ætiological features in narcolepsy common to the manifestations of the cough syndrome. It should be noted, however, that cataplectic attacks seldom are observed except in the subjects of narcolepsy. Kerr and Derbes discuss the pathological physiology of the cough syndrome, particularly with reference to the raising of the pressure in the pulmonary circuit. They believe that the actual mechanism of the attack remains unproved, and that there seems little definite in the observations and speculations germane to these dramatic attacks. It is difficult to link convincingly physiological changes in the pulmonary circuit with syncope, though the connexion of the larynx with these manifestations is suggestive.

The authors think that there are certain features of the setting of these attacks which may enhance their occurrence. They point out that the adult obese male may have a thoracic musculature capable of producing intrathoracic pressures greater than intraabdominal pressures. This, taken with other factors likely to produce stress, may be responsible for vascular readjustments in the thorax, may be of ætiological importance, and therefore may suggest preventive measures. These include excessive smoking and drinking, and those susceptible to such attacks should avoid them. One interesting point is made by Kerr and Derbes, the possibility of the cough syndrome causing dangerous episodes in traffic. Patients subject to tussive syncope have had such experiences, and though most of them appear to have had warning sufficient to avert accident this has not always been the case. Once the pattern of the syndrome has been made clear it would seem to be wise to warn the patients of the possible medico-legal aspects of any episodes which might take place on the road.

TRYPSIN IN VASCULAR DISEASES.

INTRAVENOUS and intramuscular injections of specially purified trypsin have been used to some extent for several years in the treatment of peripheral vascular and thromboembolic diseases. M. M. Fisher and N. D. Wilensky[1] have evaluated critically the safety to man of intravenously administered trypsin. Sensitivity intracutaneous tests were done in spite of the low protein molecular weight of trypsin. Patients who had no history of allergy showed no severe skin sensitivity in the 10,000 units in 250 millilitres of normal saline dilution; two out of forty-one patients showed severe sensitivity in the 50,000 unit dilution. In the 31 allergic patients four showed severe sensitivity in the 10,000 unit dilution and 12 in the 50,000 unit dilution. However, these skin tests cannot be used as criteria as to which patient will have side reactions from intravenously administered trypsin. When trypsin is given intravenously all patients should receive an antihistamine. Earlier workers used very large doses up to 250,000 units. The authors have had excellent results with an initial dose of 10,000 units diluted in 250 millilitres of normal saline or Ringer's solution, increasing up to 50,000 unit dilution on the fourth day. The infusion was administered at a rate no greater than 15 to 20 drops per minute. Improvement, when noted, usually occurs within 48 to 96 hours. If no improvement occurs within that time, further infusions are useless. Infusions were stopped with the onset of chills, headache or intestinal or chest pain. One or more of these reactions in a mild form occurred in 50% of the patients. No serious reactions were noted. The mild reactions were taken to indicate a clinical end point and are not contraindications to repeating the infusion on the following day so long as clinical improvement is noticed. Thirty-nine patients with acute thrombophlebitis were treated with intravenous infusion with a successful result in every case. Generally within forty-eight hours there was marked diminution in pain, swelling and size of the palpable thrombosis as well as in the signs of activity of infection. Other forms of peripheral vascular and thromboembolic diseases such as peripheral arteriosclerosis with or without gangrene, saddle thrombi and cerebral thrombi were treated without any success. Intramuscular injections with a preparation containing five milligrammes per millilitre in sesame oil were also tried. In six of seven patients with acute thrombophlebitis the acute symptoms and signs subsided within forty-eight hours. Three of eight patients with chronic thrombophlebitis showed temporary relief. None of the local or constitutional reactions that were observed with intravenously administered trypsin were noted with trypsin given intramuscularly, but some patients showed mild pain and nodule formation at the site of injection.

[1] *New York State J. Med.*, March, 1954.

CARCINOGENIC HYDROCARBONS IN THE ATMOSPHERE.

THE increasing incidence of lung cancer is now being much discussed. A great deal has been made of the effects of smoking, but little about the possible presence in the atmosphere of man-created pollutants from vehicular exhausts from both petrol and Diesel engines, industrial effluents from various sources including hydrocarbon emissions from petroleum refining plants and fumes from other manufacturing plants. P. Kotin, H. L. Falk, P. Mader and M. Thomas[1] have made an analysis of the atmosphere of Los Angeles and a systematic search for the sources of carcinogenic air pollutants with a view of identifying their origin and determining their ultimate fate following their emission into the air. A large volume of air was filtered through filter paper and the filter paper was extracted with thiophene-free benzene. Chromatographic separation was performed on a column of activated alumina. This revealed the presence of chrysene, pyrene, 1,2-benzpyrene, 3,4-benzpyrene and compound Y, a hydrocarbon of unknown nature. Several of these substances are known to be carcinogenic. The extract was painted on mice and many skin carcinomata developed. The 3,4-benzpyrene is present in the air in very small amounts, and it would seem that the cancers may be caused by other yet unidentified substances. Attempts to produce lung cancers in mice by inhalation of carcinogenic hydrocarbons has been generally unsuccessful. It is probable that the hydrocarbons are adsorbed to soot particles and are ineffective until eluted. In the skin this may be done by sebaceous secretions, while in the lungs there are no elutants. Under urban conditions petrol vapours and more significantly their gaseous oxidation products, in aerosol form, are present in combination with soots allowing for the simultaneous breathing of the components. A solvent has thus become available to extract aromatic polycyclic hydrocarbons from soot so as to allow their activity on the respiratory mucosa. An additional factor, which may be of considerable significance, is that of the particle size of pollutants in the air, since settling on the respiratory mucosa is obviously necessary for carcinogenesis. Aerosol particles, lying in the range between those large particles incapable of passage distal to the upper respiratory tract and those small particles which remain suspended in the tidal air, are present in urban-polluted atmosphere. Epidemiological evidence of the possibility that such atmospheric pollution is related to the incidence of lung cancer has been given by workers in the United States of America and England, who have noted a disproportionate rise in incidence in urban population groups, and it is in the urban areas that air pollution is greatest. The accelerated rate of lung cancer frequently parallels, most dramatically, the industrialization of society with its concomitant increase in air pollution. As part of a fuller investigation the authors examined exhaust products of petrol engines for carcinogenic substances. Carcinogenic hydrocarbons were demonstrated and separated. Their production under varying conditions of engine operation was determined. The amount of polycyclic hydrocarbons and soot emitted was maximal on acceleration, with the total decreasing on deceleration and idling.

[1] *Arch. Indust. Hyg.*, February, 1954.

Abstracts from Medical Literature.

GYNÆCOLOGY AND OBSTETRICS.

Marginal Insertion of the Umbilical Cord.

S. BRODY AND D. A. FRENKEL (*Am. J. Obst. & Gynec.*, June, 1953) discuss the association of marginal insertion of the umbilical cord with premature labour and early rupture of the membranes. They present a series of 32 cases, in 22 of which the membranes ruptured prematurely and early labour ensued. Fœtal distress was a frequent finding in the 22 cases, and in two instances there was vaginal bleeding during labour. The authors state that the cord may become sufficiently compressed to stop the flow of blood through it entirely, thus causing intrauterine death of the fœtus, or the vessels of the cord may rupture, causing vaginal bleeding during labour which can be mistaken for that of marginal *placenta prævia*. The authors suggest that marginal insertion of the cord may cause interference with adequate fœtal circulation, impede the nutrition of the fœtus and thus initiate labour prematurely.

Remote Effects of Cæsarean Section.

J. N. CHESTERMAN (*J. Obst. & Gynæc. Brit. Emp.*, October, 1953) analyses the records of 126 *primigravidæ* delivered by Cæsarean section and considers the remote effects in relation to (i) subsequent fertility and fecundity, (ii) rupture of the Cæsarean scar in pregnancy and labour, and (iii) the patient's subsequent gynæcological history. As a control group were selected 126 *primigravidæ* who were delivered normally. Fifty less children were born to the Cæsarean section group than to the controls; the diminished fecundity was due to "repeat" Cæsarean sections, at many of which tubal sterilization was performed. An analysis of the case histories of 1874 women who bore children after a previous Cæsarean section showed that the scar ruptured in 33 cases, an incidence of 1·76%. Rupture occurred before labour in 14 cases. In 15 cases rupture was through the scar of a lower segment operation incision; in this group there were no maternal deaths and one fœtal death. The author states that lower segment Cæsarean section is the operation of choice and is not an indication for Cæsarean section in a subsequent pregnancy. Only occasionally should the tubes be ligated at a second Cæsarean section. In the subsequent gynæcological history, hysterectomy was twice as frequent in the Cæsarean section group as in the control group.

Fœtal Position and Placental Site.

A. S. WHITEHEAD (*J. Obst. & Gynæc. Brit. Emp.*, December, 1953) presents his findings from soft-tissle placentography of 500 women examined radiologically at or after the thirty-fourth week of gestation. When the fœtal head presented, the placenta was usually implanted on the anterior or posterior wall of the upper uterine segment. In the cases of transverse or oblique lie, the placenta was most often in the fundus, in the lower uterine segment or on the anterior wall of the upper uterine segment. In breech presentations the placenta was more often found to cover one cornu of the uterus. Cornual implantation of the placenta appeared to favour persistence of breech presentation, and the author considers that it may be an important factor in determining breech presentation; however, he states that it is not the sole cause, as a breech presentation may persist irrespective of the position of the placenta.

Spinal Anæsthesia in Cæsarean Section.

DONALD W. DE CARLE (*J.A.M.A.*, February, 1954) presents an analysis of 1236 cases in which spinal anæsthesia was given successfully for Cæsarean section with no maternal mortality. All anæsthesia given in this study was administered by trained physician-anæsthetists, and a combination of procaine and tetracaine ("Pontocaine") hydrochloride as a single injection was given in each case. In view of the fact that the pregnant woman is especially vulnerable to spinal anæsthesia in amounts ordinarily employed in surgery in general, no one patient was given more than 50 milligrammes of procaine or 10 milligrammes of tetracaine; as little as 35 milligrammes of procaine or five milligrammes of tetracaine was found to be adequate in many of these cases. The preparation of an intravenous route by the anæsthetist was regarded as essential, firstly for the routine administration of fluids and, if necessary, blood, secondly for the injection of oxytocics, and thirdly for the induction of further anæsthesia when necessary. The maintenance of blood pressure normality also was the responsibility of the anæsthetist. None of the more serious post-spinal neurological complications developed in any of these cases. Four patients complained of backache at the site of injection, and 63 had moderately severe to severe headache.

Ectopic Pregnancy.

JOSEPH A. LUCCI (*Am. J. Obst. & Gynec.*, December, 1953) reports a clinical and statistical analysis of 70 cases of ectopic pregnancy from St. Joseph's Hospital, Houston, during the period 1950-1952. The general incidence was one ectopic pregnancy in 264 deliveries. Laparotomy was performed on 63 patients, one unruptured ectopic pregnancy in the distal end of the tube was removed by the aid of culdoscopy through the posterior cul-de-sac, one patient had a cervical pregnancy, and five patients passed decidual casts and were treated conservatively as suffering from tubal abortion. Pain was the outstanding symptom and was present in 68 of 70 patients. The author considers that the diagnosis of ectopic pregnancy should be guarded in the absence of a history of pain. Vaginal bleeding was present in 80% of the cases and varied from spotting to menorrhagia. An adnexal mass was present in 68% of cases. The least dependable symptom was amenorrhœa, which was present in only 23% of cases. The ectopic pregnancies were distributed anatomically as follows: tubal pregnancy, 56; tubal abortions, seven; interstitial pregnancies, four; ovarian pregnancies, two; cervical pregnancy, one. The cervical pregnancy simulated early carcinoma of the cervix and was diagnosed by biopsy and frozen section examination. Forty of the ectopic pregnancies had ruptured and 16 were unruptured. Nineteen patients were admitted to hospital in a state of shock, and the remainder had no significant shock. There were less than 3,500,000 red blood corpuscles per cubic millimetre in 18 cases and more in 52 cases. No direct correlation was observed between the number of patients admitted to hospital in a state of shock and the number of ruptured tubal pregnancies. There was, however, a direct relationship between acute shock and a red blood cell count of less than 3,500,000 per cubic millimetre. Associated pathological findings in patients submitted to operation were salpingitis (33%), ovarian cyst (28%), chronic appendicitis (13%), bilateral hæmatosalpinx (7%), endometriosis (two cases), fibromyoma (two cases). Among the diagnostic procedures in this series, dilatation and curettage were performed on ten patients, culdoscopy was employed twice, and colpotomy was performed twice. The author considers culdoscopy a valuable aid in the diagnosis of ectopic pregnancy. The four interstitial pregnancies in this series were all found ruptured at operation. One of these had progressed to a gestation of twelve weeks. There was one maternal death in this group of 70 patients. The author considers that ruptured ectopic pregnancy, with acute or chronic shock, presents a real indication for the use of intravenous ultrarapid blood transfusion. The administration of oxygen before and after operation is recommended. Nothing should be done at operation beyond the required surgery and the removal of blood and clots from the peritoneal cavity.

Interstitial Pregnancy.

LAURENCE B. FELMUS AND PAUL PEDOWITZ (*Am. J. Obst. & Gynec.*, December, 1953) report an analysis of 45 cases of interstitial pregnancy from a total group of 944 ectopic gestations, an incidence of 4·7%. There was one death in this series of 45 patients. The authors state that the term interstitial pregnancy is sometimes confused with "cornual" pregnancy and "angular" pregnancy. Early diagnosis is rare, rupture is associated with severe and rapidly developing shock, and the occurrence of rupture is often not so late as it is usually thought to be. The three possible eventualities in interstitial pregnancy are stated to be rupture into the peritoneal cavity or into the broad ligament, extrusion into the upper angle of the uterine cavity resulting in spontaneous abortion or continuation of the pregnancy to term, and finally continued development of the ovum within the substance of the uterus to term. The ætiology of the condition is obscure; there was no evidence of preexisting disease or abnormality within the pelvis in 24 of the 45 patients of the series. Among possible predisposing causes, transmigration of the ovum was noted in 26·7% of cases, pelvic inflammatory disease in 22%, and previous ectopic pregnancy, previous laparotomy and sterility in 5%. There may be no symptoms associated with interstitial pregnancy until rupture occurs, and there is then the evidence of an abdominal catastrophe. Abdominal pain was present in all the studied cases. The pain is usually mild and cramp-like at first, and increases to a peak of intensity when perforation occurs. Three-quarters of the patients gave a history of amenorrhœa, and half of them had anomalous vaginal bleeding. Profound shock following cornual perforation was

observed in 71% of cases and resulted from massive intraperitoneal hæmorrhage. The authors state that the palpation of an asymmetrical uterus with a tender cystic swelling at one or other cornu and associated abdominal pain and amenorrhœa should suggest interstitial pregnancy. The differential diagnosis includes acute degeneration of a myoma complicating pregnancy and torsion of an ovarian cyst. The treatment is by immediate surgery with simultaneous replacement of blood. Hysterectomy is often preferable to wedge resection of the lacerated cornual area, because the control of hæmorrhage is, according to the authors, more speedy and effective.

The Pregnant Diabetic.

E. TOLSTOI *et alii* (*J.A.M.A.*, November 14, 1953) discuss the management of the pregnant diabetic. Their patients were followed in a common-sense way from the time of conception. The authors state that preeclampsia, hypertension, albuminuria, retinopathy, hydramnios, œdema or ketosis may occur. Ketosis may increase towards the thirty-fifth week. If it is due to infection, that is treated; otherwise the usual supervision and treatment for a diabetic are used. Intravenous administration of 5% dextrose in water, two to three litres in twenty-four hours, may be necessary. For preeclampsia, hypertension and hydramnios, treatment is empirical. In the authors' series, if the condition regressed, Cæsarean section was regarded as the method of management of choice. One litre of 5% dextrose solution was given intravenously; 25 units of insulin were administered after 250 mils of dextrose solution had been given. Insulin was used as required. The authors point out that the child may be weak. They have an elaborate plan of treatment for the child; the basis of the plan is largely symptomatic.

Metastasis in Carcinoma of the Cervix.

RUSSELL R. DE ALVAREZ (*West. J. Surg.*, November, 1953) reports a study of 71 patients suffering from primary carcinoma of the cervix associated with remote metastasis of growth confirmed by biopsy, laparotomy, radiological study or autopsy. Generalized spread to abdominal organs and abdominal carcinomatosis are not included in the study. The average age of the patients was forty-eight years; the average duration of symptoms was 11·8 months, and the average survival rate from the time of original diagnosis was forty-eight months. The time required for progression of the growth from pelvic cancer to distant spread varied from three to twenty-nine months. The author stresses the importance of rectal examination in assessing the stage of the pelvic lesion and the importance of a careful clinical examination of all systems and radiological study to detect distant metastasis. Histological examination of the primary growths showed no correlation between the degree of cellular differentiation and the incidence of remote metastasis. Remote lymphatic spread was observed in the supraclavicular glands in 19% of cases, in the mediastinal glands in 18%, in the inguinal glands in 11·3%, and in the axillary glands in 5·6%. Metastasis in bone occurred frequently, but with no predilection of site. The most common site of bony spread was the spine, especially the lumbar region. The visceral organs most commonly involved were the lungs, liver and colon. Other organs infrequently involved were the heart, brain, spleen and breast. The author noted that bony and visceral spread occurred infrequently in patients with extensive local pelvic disease. He states that the common methods of spread of carcinoma of the cervix are by local continuity of tissue, by local or secondary contiguity, and by established lymphatic drainage routes. He considers that the distant spread to unpredictable sites is probably by vascular channels. Entry of cancer cells into the inferior vena caval system could account for the high incidence of lung involvement. Thence invasion of the pulmonary venous drainage permits a spread through the general circulation to remote sites, such as the brain, liver and bone. Another route of vascular spread may be explained by local spread of carcinoma to the large bowel and thence to the liver by the portal circulation. From the liver the growth could spread to the lung and again reach the general circulation. Another suggested method of vascular spread is by way of the vertebral vessels. The author recommends routine examination of the supraclavicular areas and careful radiological studies of all patients with carcinoma of the cervix.

Influence of Weight Gain on Pregnancy.

S. A. ALEXANDER AND J. T. DOWNS (*Am. J. Obst. & Gynec.*, December, 1953) review the recent literature on the influence of weight gain on pregnancy and report a study of 1000 unselected private patients in this connexion. These patients were on a standard diet, which was regulated according to weight gain. Salt was restricted or eliminated according to weight gain and œdema formation. All patients were routinely given some form of iron and vitamin supplement. The mean percentage weight gain in the series was 17% of initial body weight or 20 to 25 pounds. The extreme limits of weight gain during pregnancy were from nil to 49%. Patients over twenty-six years of age had a tendency to gain less than the average 17% gain, while in the younger age group equal numbers were above and below this figure. The degree of weight gain had no influence on the length of labour. Toxæmic patients had an average weight gain of 22·4%, in contrast to the 17% for the whole series. Although all patients with toxæmia had a greater-than-average weight gain, by far the great majority of patients who gained excess weight did not develop toxæmia. The authors conclude that weight gain *per se* has very little if any influence on the development of toxæmia.

ORTHOPÆDIC SURGERY.

Complications in Replacement Arthroplasty of the Hip.

HOWARD A. MENDELSOHN AND SEYMOUR L. ALBAN (*J. Bone & Joint Surg.*, January, 1954) state that a total of 53 complications occurred in 23 cases of replacement arthroplasty of the hip. Different complications were encountered which produced varying degrees of disability. There was a total of six deaths. Three occurred in the first month after operation. Five post-operative dislocations, all of the antero-superior type, occurred in the series. Four dislocations occurred in patients who had Juded prostheses, and one in a patient with an Eicher appliance. The authors believe that predisposing factors in post-operative dislocations were insufficient length of femoral neck, inadequate depth of acetabular cavity and excessive valgus placement of prosthesis. Nine patients had X-ray evidence of calcification in the soft tissues adjacent to the hip. The areas of calcification varied from slight to massive deposits surrounding the entire hip joint. Three patients complained of disabling pain at the site of protrusion of the stem from the lateral cortex of the femur. Varus deformity occurred in two cases. The prosthesis fractured in three cases. The authors state that relief from pain is the most important post-operative consideration. In their series of 40 patients, 13 have complained of persistent pain of a moderate to severe degree three to sixteen months after operation. Four patients operated upon less than three months before the time of preparation of the paper had not been evaluated from the standpoint of pain. If these four patients are excluded, one-third of the living patients have had persistent disabling pain. Included, of course, in this group of patients with persistent pain are many described as having one or more complications. Four, however, had no other complications.

Myelographic Sign of Brachial Plexus Avulsion.

JAMES C. WHITE AND JOSEPH HANELIN (*J. Bone & Joint Surg.*, January, 1954) state that when roots of the brachial plexus are avulsed, a cuff of dura-arachnoid is torn out of the spinal theca. With retraction and shrinkage of the severed stump, a cavity is created, which fills with spinal fluid. It is gradually enclosed by reformation of the ruptured arachnoid and dura, and a traumatic meningocele is formed. This can be readily filled with radio-opaque media, and the presence and extent of root avulsion can be demonstrated by myelography.

Screw Stabilization in Fractures of the Tibia.

EDGAR H. WHITE, THOMAS J. RADLEY AND NEAL N. EARLY (*J. Bone & Joint Surg.*, July, 1953) treated 66 consecutive cases of unstable fractures of the shaft of the tibia by screw fixation. Results were excellent in 44 cases, good in seven, and fair to poor in 11; four cases were not followed up. Of the 11 poor results, non-union occurred in four cases and bone grafting procedures were later necessary. In all cases the unstable fractures were treated by screw fixation; one, two or three screws were used, according to the type of fracture. The authors state that the insertion of a single screw across a fracture site results in surprising stability in many cases. They were impressed with the satisfactory results of immediate internal fixation in suitable compound fractures when treatment of the fracture is begun simultaneously with that of the soft-tissue injury. The practice of delaying definitive reduction of the fracture fragments until after the original compound injury has been converted to a closed fracture by suitable soft-tissue surgery with subsequent healing of the soft tissues has been avoided as often as feasible. The authors point out the advantage of using appreciatively less material when one or more screws are used instead of plate and screws.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XCIX.
GOUT.

GOUT has featured in medical history for a very long time, even before Hippocrates described podagra. Recognized and differentiated from other arthritides by Sydenham, himself a sufferer, it was long regarded as a disease peculiar to more affluent citizens addicted to port wine. Recent information, however, has improved our understanding of the ætiology of this condition, and better methods of treatment are available.

Incidence.

Males are more frequently affected than females, in a ratio of about 20:1. There is a strong familial incidence, although the exact genetic transmission is not yet fully understood. The actual incidence in the general population is uncertain, though probably much higher than is generally believed. Hench reported that gout accounted for 5% of all cases of joint disease seen at the Mayo Clinic.

Ætiology.

The occurrence of hyperuricæmia and tissue deposits of urates in cases of gout have been known for at least a century. Recent research has added considerably to our knowledge of the metabolism of uric acid, and it is pertinent to discuss this briefly. Uric acid is, of course, the end product of purine metabolism. Purines are derived from the breakdown of nucleic acids, which may come either from the cells of the body or from ingested food. In addition, it has been shown that purines are synthesized in the body from simpler substances, such as ammonia, carbon dioxide and glycine. While these purines may largely be used for the synthesis of nucleic acid, direct oxidation to uric acid can occur at this stage. Uric acid then is derived from purines, which are formed both from the breakdown of nucleic acids and by direct synthesis in the body. Formed uric acid circulates in the blood-stream in a concentration normally of from two to five milligrammes *per centum*. Ultrafiltration studies have shown that about one-fifth of this uric acid is in "bound" form, either in colloidal state or attached to protein. Apart from the circulating uric acid, there exists in the body a large reservoir or "miscible pool" of uric acid, which has been found by isotope studies to be of the order of 1000 milligrammes. This level is not static, there being a daily "turnover" of around 700 milligrammes of uric acid.

Mammals, other than apes and man, possess an enzyme, uricase, which converts uric acid to the more soluble substance allantoin. It seems quite definite, however, that uricolysis does not occur to any significant extent in the human body, and therefore formed uric acid can be disposed of only by excretion. The kidney treats uric acid as a threshold substance, like glucose.

In gout, therefore, the excess uric acid must presumably arise either from increased production of the substance or from diminished excretion. The exact position has not been established, but the following observations have been made. As regards excretion, it appears that, in the early stages of gout, urate clearance by the kidney is quite normal, and the average daily urinary excretion is high. Renal damage occurs in gout, however, and impaired renal function with retention of uric acid appears in the later stages of the disease.

Evidence has been produced of increased formation of uric acid in gouty subjects. Abnormally rapid formation of uric acid from dietary glycine has been demonstrated. The "miscible" pool of uric acid is considerably increased in gout, even when the serum level is still not greatly increased. Also, it has been shown that the "bound" fraction of circulating uric acid is increased, especially during an acute attack of gout.

Thus the evidence, incomplete as it is, favours the idea that gout is due to a metabolic fault which allows excessive production of uric acid. The ultimate cause of this fault remains unknown. Asymptomatic hyperuricæmia is frequently found in members of families subject to gout. In males this hyperuricæmia may develop shortly after puberty, while in females it is not usually apparent until after the menopause. It has been suggested that the tendency to hyperuricæmia is transmitted as a Mendelian dominant. Clinical gout, it is suspected, develops only when hyperuricæmia is long-standing, or is aggravated by other factors. Many attempts have been made to incriminate the endocrine system. Some workers claim to have demonstrated abnormal androgen function, while recently it has been suggested that the pituitary-adrenal mechanism is unusually insensitive to stimulation. It is of interest in this connexion that acute attacks of gout are frequently precipitated by factors such as trauma, acute infections, exposure to cold or reactions to foreign protein.

Clinical Features.

It is well recognized that the course of gout falls roughly into two stages. As Hench has emphasized, the early, or pretophaceous, stage is essentially an acute episodic arthritis with interval remission, while later the arthritis becomes chronic with occasional acute exacerbations.

The early acute attacks classically have a predilection for the metatarso-phalangeal joint of the great toe (about 60% of cases). Other joints which may be involved early include the tarsal, ankle, knee, wrist and finger joints. The affected part is swollen, extremely painful and tender, and the skin becomes shiny, showing a cyanotic erythema. Considerable distension of veins draining the area may be seen. Migratory pains may occur in other joints at this stage. Systemic disturbance is often considerable, with malaise, fever and tachycardia. There is a polymorphonuclear leucocytosis, and the erythrocyte sedimentation rate is elevated. The duration of the acute attack ranges from a few days to several weeks in very severe cases. The serum uric acid level is raised during the attack, and there is a relative increase in the "bound" fraction. Urine volume may be reduced, and a reduction in 17-ketosteroid excretion during the stage of acute arthritis has been recorded. After the attack has subsided, there may be desquamation of the skin over the affected joint, but residual joint changes are rare at this stage.

Intervals between attacks vary widely, but become shorter as the disease progresses. Ultimately permanent joint changes appear, and the patient passes into the stage of chronic gouty arthritis.

If the patient is first seen at this stage, the condition may easily be mistaken for rheumatoid arthritis or osteoarthritis. Varying degrees of deformity, disorganization and ankylosis of the affected joints may be found. Urate deposits in the tissues, or tophi, are usually found at this stage, however, and should be looked for in the helix and antihelix of the ears, in the tarsal plates of the eyes, in tendons and around the olecranon and patellar bursæ. These may ulcerate and form sinuses. Renal colic may occur owing to the passage of urate calculi, and slowly progressive renal damage is liable to develop in this chronic stage. Arteriosclerosis is common in long-standing gout, and cardiovascular complications are seen quite frequently.

The diagnosis in the chronic stage can be achieved by a careful analysis of the family history and the preceding course of the disease. The contents of tophi, when found, can be tested for sodium urate by the murexide test. X-ray examination may reveal "punched-out" areas of translucency in bone near the affected joints, or there may be extensive osteoporosis of adjoining bones. There may be extensive destruction of articular surfaces. The serum uric acid level is usually persistently raised at this stage; and even when there is nitrogen retention due to renal failure, the uric acid level is disproportionately high as compared with the urea nitrogen level. Finally, the response to treatment may be used to confirm the diagnosis.

Treatment.

In this discussion of the treatment of gout particular attention will be given to several new drugs whose introduction in recent years holds out hope of improved management of this condition.

Acute Gout.

General measures for acute gout include bed rest, with early immobilization of the affected joints, light splinting and some form of bed cradle to take the weight of bed clothes. A copious fluid intake should be ensured to assist in the elimination of uric acid, and diet should be largely carbohydrate with low fat and protein content. A number of specific measures are available, which should be employed with the object of relieving pain and aborting the attack as soon as possible.

Colchicine.—Colchicine is still the most reliable drug in the treatment of the acute attack. Its action remains a mystery. It has no effect on the renal excretion of uric acid or on the serum levels. It has been postulated that the substance inhibits the synthesis of uric acid and also reduces the "bound" fraction of circulating uric acid. This would cause a smaller turnover rate of uric acid, without necessarily altering the size of the "miscible pool". The drug should be prescribed in tablet form (grain 1/100) and one tablet taken every hour for three hours and then one tablet every two hours, without interruption, until relief is obtained. On an average, about 10 tablets are needed. Some individuals require and may tolerate up to 15 tablets, but it would be unwise to exceed this amount. The toxic effects of the drug are gastro-intestinal—nausea, vomiting and diarrhœa. Colchicine therapy should be instituted at the earliest possible moment, and a patient subject to gout should have a supply of tablets readily available. Used properly, colchicine is effective in the great majority of cases. If it is unsuccessful, or if toxic symptoms supervene, one or other of the following should be used.

Corticotrophin, Cortisone and Hydrocortisone (Compound F).—Corticotrophin, cortisone and hydrocortisone (compound F) are capable of producing very rapid remission of the acute attack, but have the disadvantage that a recrudescence may follow the withdrawal of the drugs. Corticotrophin (ACTH) is probably most effective, and 50 milligrammes should be given intramuscularly. This amount should be repeated at six-hour intervals, if necessary, until the attack is controlled. The hormone is then withdrawn gradually; for example, two injections of 25 milligrammes are followed by two injections of 10 milligrammes at six-hour intervals. It is probably better to combine ACTH treatment with colchicine, and this may be done even when the latter is ineffective alone or poorly tolerated. The first dose of 50 milligrammes of ACTH is injected, and one tablet of colchicine (grain 1/100) is given at the same time. ACTH, 50 milligrammes, is repeated once or twice at six-hour intervals until relief is obtained. Meanwhile colchicine is continued in doses of one tablet eight-hourly and maintained for about seven days.

"Butazolidin" (Phenylbutazone).—Very good results may be obtained in acute gout with "Butazolidin" (phenylbutazone); indeed, in the writer's experience, a few patients have preferred this to colchicine. The mode of action of "Butazolidin" in gout is not established, though some authors have reported increased uric acid excretion and reduced serum levels, suggestive of a renal effect of the drug. The well-known toxic effects of "Butazolidin" must be considered when the decision is being made to use this drug, but in the short-term therapy of the acute attack the risk should not be great. The drug should be given orally, two tablets (400 milligrammes) initially, followed by one tablet (200 milligrammes) every six hours until relief is obtained. Dosage of this order should not be continued for more than forty-eight hours, and the drug should probably not be exhibited at all to patients with any history of peptic ulceration or blood dyscrasia.

Chronic Gout.

The management of the interval state or of established chronic gouty arthritis is much more difficult, and the effects of treatment are naturally much less dramatic. In the light of our present knowledge, the basic principles would consist of the avoidance of factors known to precipitate acute attacks and an attempt to reduce the body uric acid content.

Despite the lack of exact knowledge of the mechanisms involved, experience has incriminated a number of factors capable of precipitating acute episodes in a case of gout. Exposure to cold or damp, acute trauma to a joint, or even unusual physical activity should be avoided as far as possible. Surgical operations are frequently followed by an acute exacerbation, which should be anticipated. It should also be remembered that a number of drugs are capable of aggravating the condition, including liver and posterior pituitary extracts, sulphonamides, mercurial diuretics, lactic acid, atropine and ergotamine. Acute exacerbations of the chronic state would, of course, be treated as described above. The following measures may be considered in the endeavour to reduce the high uric acid of the body.

Diet.—Dietary restriction, in order to reduce exogenous purine intake, has been an accepted part of treatment for many years. It is true that less uric acid appears in the urine, both in normal and in gouty persons, when purine intake is rigorously reduced. On the other hand, the demonstration that uric acid may be synthesized from simpler nitrogen compounds throws some doubt on the value of dietary restriction. It would, however, seem reasonable to avoid foods rich in purine, such as sweetbreads, anchovies, sardines, liver, kidneys and meat extracts. Alcohol intake should certainly be moderated, though there is no conclusive proof that total abstinence has any real therapeutic value in gout. The non-alcoholic fluid intake should be high in order to maintain a large urinary volume.

Salicylates.—There is definite evidence that salicylates, in large doses, promote the renal excretion of uric acid. The analgesic action is also helpful in chronic gouty arthritis. It is necessary, however, to take at least 40 grains of acetylsalicylic acid daily to cause any significant uricosuria.

"Benemid."—"Benemid" (*p*-(di-N-propylsulphonyl) benzoic acid) is an effective uricosuric agent, acting by blocking tubular resorption. It is of no value in the acute attack of gout, but is indicated in the management of the interval state or in chronic gout. There is growing evidence that, with long-term administration, the uric acid "pool" can be greatly reduced, acute exacerbations become much less frequent, new tophus-formation is prevented, and existing tophi may become smaller. Dosage recommended is 0·5 gramme daily for one week, followed by 1·0 gramme daily. This can be given indefinitely. Acute attacks may occur shortly after the commencement of "Benemid" therapy. In this event, colchicine should be used and the "Benemid" continued. Salicylates block the action of "Benemid", and these two drugs should not be used together.

"Butazolidin."—"Butazolidin" has been used with success, especially when gouty arthritis is severe. The risks of long-term therapy with this substance must be borne in mind, and the total daily dosage should not exceed 200 milligrammes.

Conclusion.

It is to be hoped that further knowledge of the ætiology of gout will suggest even more effective methods of treatment than those at present available. Even these, however, represent a considerable advance and, properly used, can provide much relief in this disabling disease.

H. N. ROBSON,
Adelaide.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on December 3, 1953, at The Saint George Hospital, Kogarah. The meeting took the form of a number of clinical demonstrations by members of the honorary medical and surgical staffs of the hospital.

Thallium Poisoning in Pregnancy.

DR. J. C. ENGLISH discussed the history of a patient suffering from thallium poisoning during pregnancy. This case is reported in full in this issue of the journal at page 780.

Hodgkin's Disease Treated with Triethylene Melamine.

Dr. English's second patient, a man, had been admitted to hospital in June, 1953, with a history of first having noticed enlarged glands in the neck two months before. Since then he had suffered from dizziness, lassitude, anorexia and night sweats. Further enlarged glands developed in both axillæ and under the chin.

On examination the patient was very pale. Large, non-tender, discrete lymph nodes were felt in both upper cervical regions, in the right submandibular and right posterior cervical regions and in both axillæ. The spleen and liver were not palpable. He had an evening pyrexia, the temperature rising to 100° to 102° F. and returning to normal or subnormal in the morning. The differential leucocyte count was as follows: neutrophile cells 73%, lymphocytes 10%, monocytes 14%, eosinophile cells 1%; the total number of leucocytes was 25,000 per cubic millimetre. Biopsy of a cervical gland showed the characteristic picture of Hodgkin's disease.

During the ensuing two months the patient was treated with TEM, approximately one tablet being given per week, during which time the white cell count fell and was maintained between 11,000 and 15,000 per cubic millimetre, the differential count being almost unaltered.

Twelve days after the patient's admission to hospital the spleen and liver were tender and palpable. Three weeks after his admission a decrease in size of all previously enlarged lymph nodes was noticed, but the liver and spleen remained enlarged. One week later, further lymph nodes in the left inguinal, occipital and posterior auricular regions became enlarged and he complained of headache. One month later the patient was discharged home, no further TEM being available.

On his readmission to hospital in September, 1953, the patient complained of pain and tenderness in both legs. He was still suffering evening pyrexia and now had generalized enlargement of lymph nodes. The spleen was also palpable. The pain in his legs was not relieved by pethidine, but he could obtain relief from "Physeptone". TEM therapy was recommenced, the tablets being given at weekly intervals.

In October the patient was referred to the Royal Prince Alfred Hospital for deep X-ray therapy, but it was considered that his condition was too widespread and a course of nitrogen mustard together with cortisone was recommended. Cortisone therapy was commenced in November in conjunction with TEM, and the patient became afebrile almost immediately and all involved lymph nodes decreased in size. At the time of the meeting the leg pains and weakness had decreased to a point at which the patient was able to spend all day out of bed on crutches, and his occasional pain could be relieved by aspirin, phenacetin and caffeine.

Torulosis.

DR. J. V. LATHAM discussed a case of torulosis and described the post-mortem findings. The patient was an elderly woman, who had been suffering from *diabetes mellitus*; the diagnosis of torula meningitis was made on the findings at autopsy, which was carried out by Dr. F. Davis. The subject was of average nutritional status. Examination of the brain disclosed that the leptomeninges were rather thickened and opaque, especially at the base of the brain, and were adherent to the dura in the region of the posterior cranial fossa. There were numerous irregular creamy-yellow plaques, about the size of miliary tubercles, in the leptomeninges, scattered diffusely over the surface of the brain, and most pronounced in the region of the cerebellum. The cerebellar tissue itself was softened. The ventricular system contained purulent cerebro-spinal fluid and the walls of the ventricles were softened. The left choroid plexus was swollen and gelatinous. Fairly severe atheroma was present in the arteries at the base of the brain. No abnormality was detected in the lungs and pleural cavities. The abdomen was not examined. Examination of a wet film prepared from the purulent cerebro-spinal fluid disclosed *Torula histolytica*. Microscopic examination of five sections of brain revealed extensive invasion by *T. histolytica*, which had produced numerous ulcers and abscesses of varying size.

Pulmonary Tuberculosis in a Child Aged Ten Months.

DR. B. HANEMAN showed a child who, at the age of ten months, had become feverish and irritable and had suffered from night sweats and a mild cough. Within seven days he had developed rubella; but when his symptoms did not subside, further investigations were carried out. There was a family history of pulmonary tuberculosis. The Mantoux test was carried out and a reaction 2·0 centimetres in diameter followed the injection of 0·1 cubic centimetre of 1:100 tuberculin. A full blood count and examination of the cerebro-spinal fluid revealed no abnormality. Tubercle bacilli were grown in culture from the gastric fluid.

On August 8, 1952, X-ray examination revealed consolidation in the upper lobe and in the apical segment of the lower lobe of the left lung. Six days later the appearances in the film suggested that the consolidation was not so dense. On August 28 consolidation was present in the upper segment of the lower lobe of the left lung; an abscess cavity was visible and the heart was slightly displaced to the left. On September 8 the area of dullness was unchanged; the air-containing cavity was smaller. On September 22 the cavity had cleared; dullness was still present in the upper half of the lower lobe of the left lung, and left hilar adenopathy and narrowing of the left main bronchus were apparent. By December 15 the area of dullness had extended to the periphery in the antero-posterior view; an area of cavitation was still present. On January 12, 1953, the cavitation was not so obvious as previously. On February 12 it was noticed that the left lung did not deflate so much as the right; pressure on the left main bronchus was postulated. At about that time the parents noted a whistle in the child's breathing. By August 13 the lesion had decreased in size and was harder in character; the suggestion was that the lesion might go on to calcification. On September 29 multiple small areas of calcification were visible.

Dr. Haneman said that the child had been treated with streptomycin and PAS for almost a year. During that time he had had several upper respiratory tract infections, which were treated with sulphonamides and with penicillin given by mouth. To all outward appearances, at the time of the meeting he was perfectly well. It was considered that he had an extensive primary tuberculous complex, which was going on to calcification. A bronchographic examination at a later date would reveal whether any bronchostenosis had resulted. Of interest on that point was the article by Howard Williams and Charlotte Anderson on "Bronchiectasis and Bronchostenosis following Primary Tuberculosis in Infancy and Childhood", in *The Quarterly Journal of Medicine* (1953, New Series, 22:261).

Hæmolytic Anæmia Cured by Splenectomy.

Dr. Haneman's second patient was a male, who had been admitted to hospital in January, when aged eight years. Four days earlier he had developed a headache, and on the next day fever and abdominal pain. The fever continued, the abdominal pain increased, and on the day of his admission to hospital he was vomiting. In contrast to the other members of a healthy family, the boy was pale and puny and had always had similar recurrent attacks, characterized by headache, fever and abdominal pain. They occurred at intervals of several months, were self-limiting (lasting about three days) and left the child pale and weak. The present attack was more severe than usual.

On examination the patient was very pale, had an icteric tinge and appeared to be in pain. His temperature was 104·2° F. and his pulse rate 150 per minute. He had a stiff neck and Kernig's sign was elicited. The tip of the spleen was palpable and there was slight generalized lymph gland enlargement. There was a suspicion of tenderness round McBurney's point. Lumbar puncture revealed no abnormality, and penicillin therapy was started. A blood count gave the following information: the erythrocytes numbered 1,800,000 per cubic millimetre, the hæmoglobin value was 5·6 grammes *per centum*, and the indices were normal; no reticulocytes were seen. The leucocytes numbered 3600 per cubic millimetre. An erythrocyte fragility test showed that hæmolysis commenced in 0·51% saline and was complete in 0·3% saline.

At this stage the clinical picture was one of leuchæmia or infectious mononucleosis. In view of the patient's severe anæmia he was given a transfusion of packed cells; thereafter his general condition soon improved. Within a fortnight of his admission to hospital his hæmoglobin value was 14·2 grammes *per centum*. The Paul and Bunnell test for infectious mononucleosis produced a negative result. The following tests also all produced negative results: agglutination tests against *Salmonella typhi* H and O, *S. paratyphi* A, B and C (H antigens), Proteus OX19, Proteus OXK and *Brucella abortus*, and the Wassermann test. The direct Van den Bergh test result was negative; the quantitative Van den Bergh test gave results of 1·7 milligrammes of bilirubin per 100 millilitres of serum before any blood transfusion had been given.

One month after this acute episode the patient's spleen was firm and easily felt four fingers' breadth below the costal margin. A month later it was palpable only two fingers' breadth below the costal margin. The boy complained of an ache in that area on running; by that time he was becoming pale and breathless again. The hæmoglobin value had fallen to 9·6 grammes *per centum* and the erythrocytes to 3,400,000 per cubic millimetre (reticulocytes 0·5%); spherocytes were reported present on that occasion for the first time. A bone marrow biopsy was taken from the iliac crest; Dr. A. E. Gatenby reported hyperplasia of erythroblastic elements in keeping with acholuric jaundice, but no evidence of leuchæmia.

In April the patient's spleen was removed; it was twice the normal size. Microscopic examination of sections revealed extreme congestion of the pulp with obliteration of sinuses, the findings being in keeping with the diagnosis of congenital hæmolytic anæmia. Examination of the lymph glands revealed simple reactive hyperplasia.

Dr. Haneman said that at the time of the meeting the child was enjoying good health. Two days previously the direct Van den Bergh test had produced a negative result, the result of the quantitative Van den Bergh test was 0·4 milligramme per 100 cubic centimetres, the erythrocytes numbered 4,200,000 per cubic millimetre, and the hæmoglobin value was 13·1 grammes *per centum*. Splenectomy had been performed because the anæmia and its recurrent hæmolytic crises were interfering with the child's health. A puzzling feature of the case was the absence of reticulocytosis.

Dissociated Anæsthesia.

DR. J. S. BOXALL and DR. K. C. JACKSON showed two patients suffering from dissociated anæsthesia.

The first patient was a male, aged sixty-two years, who had had a thrombosis of the posterior inferior cerebellar artery. He had been admitted to hospital on September 3, 1953, with right-sided headache, vomiting, diplopia, incoordination of the legs and veering to the right so that he was unable to sit or stand. He had hiccups and a husky voice. Numbness was present on the right side of the face and the left side of the body. He had not lost consciousness. There had been sweating of the right side of the face, followed later by the absence of sweating. He had had a similar milder attack two months earlier. A shrapnel wound in the right arm had been sustained in 1917.

The signs and symptoms were as follows. Related to the nervous system on the same side there were pain on the right side of the face and loss of pain and temperature sensation; touch sensation was retained. Diplopia was present on looking to the right. Vertigo and vomiting were present, but no deafness was noted. There was no loss of taste in the posterior third of the tongue. The palate moved normally. Some dysphagia was present, the right vocal cord was paralysed and the voice was husky. The pupil was small and ptosis and enophthalmos were present. Sweating was absent. Ataxia of the limbs and an unsteady gait were present, with falling to the right. Related to the nervous system on the opposite side (the left) the signs and symptoms were loss of pain and temperature sensation, the face included. In relation to the mesial fillet and pyramidal tract, touch and postural sensibility were unaffected, as were power and the reflexes.

It was pointed out that X-ray examination of the skull revealed no abnormality, and the urine was found to be normal. The blood pressure was not raised. The cerebrospinal fluid was clear, the constituents were normal, and it did not react to the Wassermann test. At the time of the meeting the ataxia was diminishing so that the patient could walk. The usual permanent sequelæ were sensory loss over the face on the side of the lesion, partial Horner's syndrome, and loss of pain and temperature sensation on the opposite side of the body.

The second patient shown by Dr. Boxall and Dr. Jackson was a female, aged twenty-two years, who on October 14, 1953, had noticed numbness of the right leg, slowly increasing over the ensuing twenty-four hours. Her menstrual period had just finished. Her own doctor had noticed dissociated anæsthesia of the whole of the right lower limb to the level of the tenth thoracic segment; a heated pin which he applied to her calf raised a blister without causing her pain. Three weeks later the level of sensory loss had risen to the level of the seventh thoracic segment. Two weeks prior to her admission to hospital it was found to have extended to the level of the first thoracic segment. Apart from a little heaviness and latterly some burning pain in the right leg, she felt as well as ever, and had continued with her normal duties. She was a smoker and had had a cough for four years. On being questioned she said that she had had headaches for three months. She did not appear to be worried about her condition. She had three children, aged respectively four, three and two years. Her menstrual periods lasted for seven to twenty-one days, and occurred at intervals of ten to twelve days. She had undergone an appendicectomy six years earlier.

On examination of the patient it was found that pain and temperature sensation on the right side of the body was lost from the shoulder down, the ulnar border of the forearm included. Vibration sense seemed to be slightly impaired. Her response to touch, sense of position, motor power, reflexes and tone were normal. No abnormality was detected in the cranial nerves and optic fundi. The patient had no deformities. A blood count gave the following information: the hæmoglobin value was 105%; the leucocytes numbered 14,700 per cubic millimetre, 65% being neutrophile cells, 22% lymphocytes, 6% monocytes and 7% eosinophile cells. Her temperature was normal. Her systolic blood pressure was 120 millimetres of mercury and her diastolic pressure 80 millimetres. X-ray examination of the spine revealed no abnormality in the thoracic or lumbar region. X-ray examination of the chest revealed no abnormality except slight bronchitic changes. The cerebrospinal fluid was normal and gave a negative response to the Wassermann test.

The comment was made that if the lesion was of organic origin it must be a rapidly extending lesion of the left spino-thalamic tract, for example hæmatomyelia or syringomyelia. Hysteria, disseminated sclerosis and neoplasm had also to be excluded.

Pancreatogenous Steatorrhœa Associated with Mumps.

DR. G. C. WILSON showed a male patient, aged thirty-six years, who had suffered from steatorrhœa for six months and had lost 18 pounds in weight in that period. He had had abdominal pain for six months, mainly in the lower part of the abdomen. He had had a duodenal ulcer, diagnosed two years earlier, and had undergone appendicectomy eight years earlier. Two years prior to the meeting his left testis had been swollen for six months, and he had worn a truss for one year. Six months prior to the meeting he was well, when he began to suffer from lower abdominal pain, at times very severe, occurring even with micturition and occasionally relieved by defæcation, and from the passage of "oil" *per rectum* (the "oil" appeared first and was followed by a pale, watery or poorly formed stool with an offensive odour). The comment was made that in that connexion it was of interest that in Bodansky's "Biochemistry of Disease" it was stated that in pancreatogenous steatorrhœa the fatty element of the stool was at times so severe that neutral fat would separate out as a yellowish oil. It was important to recognize that as strongly presumptive evidence of pancreatic disease, and not due to medication. That phenomenon was not found in steatorrhœa caused by such conditions as sprue, or in idiopathic steatorrhœa. The patient also suffered from the loss of 18 pounds in weight in six months. His appetite was good, but fatty foods seemed to disagree with him. He had never had melæna or passed bright blood *per rectum*. He had had no back pain and no vomiting. About eighteen months prior to the meeting he suffered from epigastric pain, and peptic ulcer was diagnosed; at that time he lost 16 pounds in weight and regained his weight on the ulcer régime. At that time steatorrhœa was present, the stool being thin and pale, but containing no oil.

On examination of the patient, tenderness was present over the duodenum and possibly over the pancreas; tenderness was also elicited on rectal examination. The only glandular enlargement was a firm, discrete enlargement of the left axillary group. The spleen and liver were not enlarged. A number of investigations were carried out. A blood examination gave the following information: the hæmoglobin value was 12·7 grammes *per centum*; the leucocytes numbered 3900 per cubic millimetre, 58% being neutrophile cells, 2% eosinophile cells, 35% lymphocytes and 5% monocytes; the blood sedimentation rate estimated by the Wintrobe method was 41 millimetres in one hour. The fæces were examined; the stool was bulky, pale and unformed, and had a foul rancid odour; undigested food residue was visible. The total fat in the dried fæces was 41%; 53% was split fat and 47% unsplit fat. The pathologist, Dr. C. B. Cox, reported that the stool appearances and analysis suggested a pancreatic deficiency, but malabsorption might also be a factor. X-ray examination after a barium meal revealed deformity of the duodenal bulb almost certainly secondary to an old ulcer; the follow-through examination revealed no evidence of stasis. A barium enema was given and an X-ray examination carried out. The enema ran freely from the rectum to the caecum and through the ileo-caecal valve; the sigmoid colon was elongated and redundant, but no other abnormality was seen. A glucose tolerance test produced a diabetic type of curve. No pathogenic organisms were grown on culture from the stools, and no occult blood was detected in them. The serum bilirubin content was 0·6 milligramme per 100 millilitres. The serum calcium content was 10·3 milligrammes per 100 millilitres. At the time of the meeting no X-ray examination of the gall-bladder had been carried out, the serum amylase content had not been estimated, and the duodenal contents had not been examined.

Epidermolysis Bullosa with Œsophageal Stricture.

Dr. Wilson then showed a patient suffering from *epidermolysis bullosa* and discussed the condition. He said that it was a rare disorder of the skin, the essential element of which was the appearance of blisters, most frequently on the distal parts of the extremities, after trauma. There was a familial tendency to the disease. Bullous lesions of the membranes and dystrophy of the nails *et cetera* were often associated. *Epidermolysis bullosa* might be congenital or acquired. There were two types, *epidermolysis bullosa simplex*, and dystrophic *epidermolysis bullosa*. The *simplex* form was often present at birth in the form of blisters on the feet, or it appeared during infancy, and it tended to persist throughout life; the duration of the blisters was from two to ten days. Nikolsky's sign was often present, and in 2% of cases the mucous membranes were affected. The patients were well built and of normal height and weight; their hair, nails and teeth were normal. The hereditary tendency was usually obvious. Dermatographism and hyperidrosis were often present also.

Dr. Wilson went on to say that allied to the dystrophic form of the disease were recurrent bullous eruptions of the feet, occasionally the palms; the eruptions had the appearance of blisters and were associated with pressure from footwear and the use of tools and instruments. Hyperidrosis was always worse in the summer. The blisters remained for a few days and healed without scarring. The dystrophic form of the condition was of two types, dominant and recessive. The dominant type was very rare; it was the type from which the patient being shown was suffering. It was intermediate between the *simplex* and recessive types. The patients were usually well built and had normal hair and teeth; the nails might be normal. Blisters followed trauma on the hands, forearms, legs and feet; they usually healed perfectly or by scarring. Occasionally blisters occurred in the mouth. Hyperidrosis and dermographism were the rule. The recessive type was much more severe than the *simplex* form or the dominant type, and was the commoner type of the dystrophic form of the disease. The lesions were present at birth or shortly afterwards. Survival beyond infancy was rare; most patients had died by the time of puberty. If they survived, such patients were small and mentally subnormal, and usually showed all the following features: scars on the feet, ankles, knees, hands, elbows and forehead; epidermal cysts, particularly on the hands; some degree of involvement of the mucous membranes (always present), the blisters often being hæmorrhagic; occasionally alopecia; affected conjunctivæ and corneæ; late eruption of teeth; hyperidrosis; hyperpigmentation and depigmentation.

The patient shown by Dr. Wilson was a male clerk, aged forty-five years, who had had since birth a tendency to the formation of blisters on slight to moderately severe trauma on the legs, the ankles, and the dorsal aspects of the feet and hands, as well as the forearms and elbows. In the skin a shearing force was necessary to produce the lesions, and simple pressure would not induce them. Firm twisting of the skin of the wrists, as in wrestling, would strip the superficial layers of the skin back (Nikolsky's sign). The hands and palms were never involved. The hair was normal. The patient was normally developed and his intelligence seemed above average. The lesions had no tendency to suppurate, and he was less susceptible to minor skin infections than most people. He had served in the army for six months and had noticed that he was one of the few not affected with tinea. He had pronounced hyperidrosis of the palms and soles, which were not involved by blisters, even when he was an infantryman. The blisters varied in diameter up to two or three inches and were raised one-quarter of an inch to half an inch; they contained clear fluid, which he released soon after their appearance, with prompt healing and some scarring. The medial aspect of the ankles was the most troublesome site. Dystrophy of the finger and toe nails was present. He was in the habit of paring them back and cutting back the horny layers which tended to develop. Two of the nails had become affected during his life. One nail was normal. Crossing his legs and sliding one over the other were sufficient to cause large blisters to develop after twenty-four hours or so; they lasted for seven to ten days. For eleven years he had developed similar blisters, of sudden onset, on the dorsum of the tongue and on the gums, which tended to be hæmorrhagic. No other part of the mouth or pharynx had been involved, and there were no known precipitating factors, such as foods. Trauma did not seem to be a factor. He had been subject to dental sepsis and had worn an upper denture since the age of nineteen years. His lips had never been involved nor had his eyes. He had had various treatments for the mouth lesions and thought that vitamin *C* had been the most effective. Since childhood he had had difficulty in swallowing liquids "in a straight draught". This condition had become much more acute, and five years prior to the meeting he had had attacks of vomiting and of obstruction to swallowing, so that he was unable to swallow food or saliva until an obstruction had been removed. X-ray examination with a barium bolus had revealed considerable narrowing very suggestive of carcinoma. Three œsophagoscopic examinations with dilatation, carried out by Dr. H. B. Harwood, had relieved his symptoms for the past two years. Examination of a biopsy specimen had given negative results. Since then occasional difficulty with swallowing had occurred with large pieces of solid food only. His previous history was otherwise irrelevant. The only family history obtainable was that his father had had similar dystrophy of the nails, feet and hands throughout his life; he also had a notable disregard of infection, and treated potentially septic gardening abrasions in cavalier fashion. He was aged seventy-two years, and active. On examination he was found to have dystrophy of the nails identical with that affecting his son. He had no tendency to the formation of blisters, and no buccal lesions.

Dr. Wilson commented that the case was presented as an example of dystrophic *epidermolysis bullosa* of the dominant type, associated with an œsophageal stricture. A search of the literature had failed to disclose any previous case reports of a similar association, though the association of *epidermolysis bullosa* and bullous buccal lesions was well recognized. Moreover, the occurrence of benign mucous membrane pemphigoid lesions with œsophageal stricture had been reported on nine occasions (*Medicine*, February, 1953). The present case emphasized the close relationship between those conditions and the difficulties associated with classification; it supported the opinions of Sachs, Hyman and Gray (*Arch. Dermat. & Syph.*, 1947, 55: 91) that familial benign chronic pemphigus (Hailey and Hailey) was really a variant of *epidermolysis bullosa*. The case under discussion, though one of great rarity, seemed to link the benign type of pemphigus very closely with *epidermolysis bullosa*, since it appeared to relate the buccal lesions of benign mucous membrane pemphigoid to those of *epidermolysis bullosa*, through the presence of an œsophageal stricture.

Bilateral Adrenalectomy for Metastatic Mammary Carcinoma.

DR. T. E. WILSON discussed the case of a female patient, aged fifty-four years, who had undergone a radical mastectomy in January, 1951, for carcinoma of the left breast. In February, 1952, she developed a pathological fracture of the left femur and was treated by Dr. A. L. Webb in a plaster cast for nine months and with testosterone given both orally and by injection. When she was discharged from hospital in November, 1952, union had occurred, but within a month she was complaining of pain in the back. Despite continued therapy with testosterone this pain greatly increased in severity, and on July 3, 1953, she was readmitted to hospital. An X-ray examination then revealed collapse of the eleventh thoracic vertebra and metastases in the tenth thoracic vertebra and in the left tenth rib. There was then no evidence of any lesion of the spinal cord. Testosterone propionate was given by injection (100 milligrammes daily for seven days, then thrice weekly). Methyl testosterone was also given orally (20 milligrammes twice daily). Despite increasing doses of morphine and pethidine the pain continued to increase.

On July 29 bilateral adrenalectomy was performed through the beds of the twelfth ribs. During the operation "Neo-Synephrine" was given in doses of one minim as required. The administration of cortisone acetate (50 milligrammes given intramuscularly), of DOCA (five milligrammes given intramuscularly), and of sodium chloride (five grammes given orally) had been started three days before the operation. On the day of the operation 150 milligrammes of cortisone and five milligrammes of DOCA were injected before the operation, and injections of cortisone were given every four hours after the operation. On the following day 50 milligrammes of cortisone were given four times, and on the next day this dose was given twice. Thereafter, 50 milligrammes of cortisone were given orally each day. The injections of DOCA were repeated on only the two days after operation. On July 31 the patient's serum sodium level was 281 milligrammes per 100 millilitres. On August 16 the cortisone dosage was increased to 100 milligrammes for two days and it was given by injection, as she was complaining of nausea, palpitation and weakness. Her systolic blood pressure had fallen from 135 to 110 millimetres of mercury and her diastolic blood pressure had remained 90 millimetres of mercury. The dosage of cortisone was then reduced again to 50 milligrammes given daily by mouth. A further X-ray examination some time later also showed extensive metastases in the tenth thoracic vertebra and in several ribs. After the operation no difficulty was encountered with the maintenance therapy with cortisone *et cetera*. The pain in the back was considerably diminished after the bilateral adrenalectomy, but the metastases continued to progress, and by October 29 complete paraplegia had developed. Her condition thereafter rapidly deteriorated, and death occurred on November 9.

Laryngectomy.

Dr. T. E. Wilson's next patient was a man, aged fifty-two years, who had been admitted to the Saint George Hospital on September 21, 1953, complaining of increasing huskiness of the voice of four years' duration. A biopsy of the lesion of the vocal cords showed an epidermoid carcinoma; this involved the anterior end of each vocal cord and extended forward to the base of the epiglottis. No lymph glands were palpable.

On September 23, under "Pentothal", "Scoline", and ether given by the intratracheal route (Dr. A. H. Hodge), total laryngectomy was performed. After the gap in the pharynx

had been repaired with interrupted sutures of chromicized catgut a Wangensteen tube was inserted down the pharynx and œsophagus for feeding. After two days the tracheotomy tube was removed and at no time did the patient have any difficulty with breathing. For the first four days after operation his temperature was elevated to 100° F.; thereafter it was normal.

Within a month of operation he was able to swallow fluids and a light diet, and on October 30 he was discharged home. The wound was healed, he was swallowing without difficulty, and he did not suffer from dyspnœa. He was later referred to a speech therapist. Dr. A. E. Gatenby, the pathologist, reported that the excised specimen was a larynx with the left lobe of the thyroid gland and two lymph glands attached. There was a small friable growth involving half the anterior end of each vocal cord and extending forwards to the base of the epiglottis. Microscopic examination of a piece of the tumour revealed an epidermoid carcinoma. No malignant involvement was seen in the epiglottis or in the two lymph glands located in the attached connective tissue.

Benign Gastric Ulcer Penetrating the Spleen.

Dr. T. E. Wilson then showed a married woman, aged forty-seven years, who had complained of increasing upper abdominal pain present for six months. The pain was not related to meals, but was partly relieved by antacids. During that time she had lost ten pounds in weight. Examination of the patient revealed no abdominal mass or tenderness. On August 6, 1953, the radiologist reported after a barium meal X-ray examination that there was a filling defect about three inches in diameter with ulceration on the greater curvature near the fundus of the stomach, which was almost certainly a carcinoma.

On August 14 a Billroth I gastrectomy and splenectomy were performed. The spleen and stomach were firmly adherent. There was no evidence of metastases. The pathologist's report on the excised specimen was as follows: "The specimen consisted of the distal two-thirds of the stomach with the spleen adherent to the left posterior surface. In this situation there was a chronic peptic ulcer 3·0 centimetres by 2·5 centimetres and 3·0 centimetres deep. The medial surface of the spleen formed the floor of the ulcer. Microscopic examination confirmed the diagnosis of chronic peptic ulcer. Scar and granulation tissue in the floor of the ulcer blend with the capsule of the spleen and in one situation the ulcer extends into the splenic substance. No evidence of carcinoma has been found." Dr. Wilson said that since the patient had been discharged home on August 26 her condition had improved and she had been symptom-free.

Atypical Carcinoma of the Rectum.

The next patient shown by Dr. T. E. Wilson was a married woman, aged sixty-seven years, who had complained of some irregularity of the bowels for one month prior to her admission to hospital on January 1, 1953; otherwise she had been well. Examination of the patient revealed a roughened, ulcerated area, about two inches in diameter, in the rectal mucosa over the posterior part of the ano-rectal ring. Although no tumour was palpable and there was no fungation of the edges of the ulcer, examination of a biopsy specimen showed the lesion to be an adenocarcinoma of the rectum.

On February 11 a perineo-abdominal excision of the rectum together with the adherent posterior vaginal wall was performed. Convalescence was uneventful and the patient had remained well since then. Dr. Gatenby's report on the excised specimen was as follows: "The sigmoid colon showed extensive diverticulosis. The mucosa of both the rectum and sigmoid colon appeared to be atrophic, and two inches above the anus a roughened area of mucosa overlying a thickened wall could be seen, but no distinct tumour could be identified. One piece of this area and one piece of the sigmoid colon showing a diverticulum were sectioned. Microscopic examination showed the presence of adenocarcinoma in the roughened area of mucosa. The diverticulum from the sigmoid colon did not show unusual microscopic features."

Vesico-colic Fistula.

Dr. T. E. Wilson finally showed a married woman, aged sixty-eight years, who had been admitted to the Saint George Hospital on August 14, 1953, complaining of frequency of micturition and scalding of four months' duration (despite treatment with "Sulphatriad" and potassium citrate), of lower abdominal pain present for two months, and of the passage of fæces in the urine of six weeks' duration. Her past history included a total hysterectomy in 1933. A barium enema X-ray examination made on November 29, 1945, had shown "appearances suggestive of diverticulitis". On June 29, 1953, her urine had contained a few pus cells, red cells and coliform organisms. When she was admitted to hospital she was overweight, and tenderness was present in the left iliac fossa. On August 15 a cystoscopic examination revealed fæces in the bladder, but no definite fistula was seen. A transverse colostomy was established on August 26 and an inflammatory mass was then palpable in the pelvis and the sigmoid colon contained inflamed diverticula. X-ray examination with a barium enema on September 25 revealed a small fistula from the sigmoid colon to an area anterior to it.

On November 11 the vesico-colic fistula was found to extend between the fundus of the bladder and the sigmoid colon. After separation the opening in the bladder (which had closed) was oversewn and about eight inches of the sigmoid colon containing the other end of the fistula were resected. Continuity of the bowel was restored by a two-layered end-to-end anastomosis. As the omentum was too short to bring down into the pelvis, that portion of the bowel containing the anastomosis was brought down into an extraperitoneal position. For the next six days the bladder was drained by an indwelling catheter. The colostomy was to be closed in one month.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

AN ENCOUNTER WITH A NATIVE DOCTOR.[1]

STRETCHED out at ease before our fire all sides continued to chat and entertain each other. Gombeeree showed us the mark of a wound which he had received in his side from a spear: it was large, appeared to have passed to a considerable depth and must certainly have been attended with imminent danger. Perhaps the relation given by Gombeeree of the cure of his wound now gave rise to the following superstitious ceremony. While they were talking Colbee turned suddenly round and asked for some water. I gave him a cup full, which he presented with great seriousness to Yellomundee as I supposed to drink. This last indeed took the cup and filled his mouth with water, but instead of swallowing it, threw his head into Colbee's bosom: spit the water upon him: and immediately after, began to suck strongly at his breast below the nipple. I concluded that the man was sick and called to the governor to observe the strange place which he had chosen to exonerate his stomach. The silent attention observed by the other natives however soon convinced us that something more than merely the accommodation of Yellomundee was intended. The ceremony was again performed: and after having sucked the part for a considerable time the operator pretended to receive something in his mouth which was drawn from the breast. With this he retired a few paces, put his hand to his lips and threw into the river a stone which I had observed him to pick up slyly and secrete. When he returned to the fireside Colbee assured us that he had received signal benefit from the operation and that this second Machaon had extracted from his breast two splinters of a spear by which he had been formerly wounded. We examined the part but it was smooth and whole: so that to the force of his imagination alone must be imputed the wound and its cure. Colbee himself seemed nevertheless firmly persuaded that he had received relief and assured us that Yellomundee was a Cár-ad-ye or Doctor of renown. And Boladeree added that not only he but all the rest of his tribe were Cár-ad-yee of special note and skill.

The Doctors remained with us all night sleeping before the fire in the fullness of good faith and security.

[1] From "A Complete Account of the Settlement at Port Jackson", by Watkin Tench (1791). Tench was one of a party headed by Governor Phillip and including two natives, Colbee and Boladeree, which left Sydney in April, 1791, to ascertain whether the Hawkesbury and the Nepean were in fact the same river. He describes an encounter with some other natives. From the original in the Mitchell Library, Sydney.

Correspondence.

THE FELLOWSHIP OF CHRISTIAN HEALING.

SIR: I have read with great interest Dr. Hull's letter on the Melbourne conference of the Fellowship of Christian Healing in your issue of April 24, 1954. I can quite understand his point of view, which was more or less my own until a few years ago, but an interest in psychiatry and deeper spiritual experience have caused me to change that view. For this reason, and also because I was one of the speakers at that conference, may I make some comments?

Jesus Christ did indeed come primarily to save the souls of men, but He was also the Great Physician who healed their bodies and minds, and His healings were both glimpses and signs of the Kingdom of God on earth. His methods were probably more "scientific" than we yet realize, and though apparently simple, probed deeply and powerfully. Often healing of the body and mind was accompanied or preceded by healing of the soul, the body, mind and soul being inextricably interwoven in our earthly life.

It is the concept of this amalgam of body, mind and soul that prompts those of us who would like to see more cooperation between clergymen and doctors. I gather from Dr. Hull's letter that he is opposed to organized cooperation between the two professions. Is he opposed to an individual clergyman and doctor cooperating to help a particular patient? And if he is not, why cannot organized cooperation and the pooled knowledge of many clergymen and doctors help to solve the numerous problems awaiting solution in this field? No one is advocating a "bastard course in medicine" for clergymen so that they can become doctor-substitutes ("an army of quacks"), but we do advocate that clergymen and doctors get together to learn more about the contribution each profession can make towards helping people to live healthier lives.

It is precisely because clergymen know more about the soul than doctors, and because doctors know more about the body and mind than clergymen, that cooperation is urged. They can help each other to help their patients, body, mind and soul—if the patient wants such help, of course, and one finds in practice that many patients do come to doctors with dis-ease of the soul as well as of the body and mind. Should we fob them off with sedatives? Or should we offer them the combined resources of modern medicine and enlightened theology? The Council of the British Medical Association in England has signified its approval of the latter course, and in 1947 stated (*Supplement to British Medical Journal*, November 8, 1947): "There is no ethical reason to prevent medical practitioners from co-operating with clergy in all cases, and more especially those in which the doctor in charge of the patient thinks that religious ministrations will conduce to health and peace of mind or lead to recovery. Such co-operation is often necessary and desirable, and would help to prevent abuses which have arisen through the activities of irresponsible and unqualified persons." The remainder of this statement is worth reading in full.

So far, in cooperating with clergymen, I have found most of them just as humble in their approach to the medical profession as we should be to theirs. On the whole, they do not wish to become "quacks", and their thinking has certainly progressed far beyond that of their ancestors of the fifteenth century. They do not use "incantations, phylacteries, amulets, holy relics" *et cetera*. They do use prayer, and it is the prayer of faith that links us with the healing love and power of our Creator.

Yours, etc.,

B. H. PETERSON.

Mental Hospital,
Morisset,
New South Wales.
April 27, 1954.

SIR: Concerning the Fellowship of Christian Healing. Surely nothing further than the present freedom of access of chaplains to patients in their homes and in hospitals can be welcomed by the profession. An ancillary arm of spiritual healers and faith healers is dangerous indeed. I do firmly believe that no sincere and able chaplain would wish to equip himself with an imperfect medical knowledge, so that he would in any way change his present relationship with a patient, and so imperil the present harmony between chaplain and physician.

The fully integrated man and woman, in serious illness, takes stock of his and her supernatural life as well as natural life. Chaplain and physician then work together for the whole restoration of the individual. Every physician has experienced the extraordinary calm and courage of the simple devout in the face of serious illness and death. The peace of mind that can only come from peace of soul is a mighty sedative.

Statements by Dr. W. J. Hull in your issue of April 24, 1954, deserve comment. "Christ came to save the souls and not the bodies of men"—agreed—but He showed Himself intensely interested in their physical welfare. He cured the lame, the blind, the dumb, the issue of blood, the lepers, the palsy; He restored the cut-off ear of the soldier. He comforted the tortured mind of the prostitute Magdalen. "He taught neither science nor medicine and probably knew little about either." Christ claimed and by His Resurrection proved He was God. His mission was neither scientific nor medical. If Dr. Hull really means "He knew little of either", he either has a very limited concept of the infinite knowledge of God or he does not believe in Christ. It is a mistake to think of Christ as a period piece, a treasured memory of the past. He Himself said: "Before Abraham was, I am." The Christology of Saint Paul is the living and eternal Christ perpetuated as the head of His Mystical Body—the Church.

Yours, etc.,

LOUIS H. MCCAFFERY.

Goulburn,
New South Wales,
April 27, 1954.

SIR: I read with interest the report of the meeting of the Fellowship of Christian Healing, held in Melbourne and published in THE MEDICAL JOURNAL OF AUSTRALIA, March 20, 1954, and also the correspondence of the issues dated April 17 and 24, relative to the above.

The letter of April 17 has my full support; while agreeing and endorsing most of the letter of April 24, I deplore the last sentence of the third paragraph and the first sentence of the last paragraph.

My sincere wish is that the Fellowship will base all its future activities on the sure foundation of the scriptures, quoting *Ecclesiasticus*, chapter 38, verses 1 to 15, with special attention to verse 14, and *St. James*, chapter 5, verses 14 and 15.

Yours, etc.,

J. PARKES FINDLAY.

143 Macquarie Street,
Sydney,
April 28, 1954.

SIR: I do not intend to enter into a discussion concerning the Fellowship of Christian Healing, but I do feel that the letter of Dr. Walter Hull (M. J. AUSTRALIA, April 24, 1954) requires an answer in the interests of historical accuracy.

It is rather a rash statement to say that Hippocrates was the greatest physician of all time. During the fifth and fourth centuries B.C. there was a great upsurge of intellectual activity, and Hippocrates did for medicine what Plato, Parmenides and Heraclitus did for philosophy. He was a keen observer and a deep thinker, and founded a system of medicine as the others founded systems of philosophy.

The statement that "the conquest of Greece by the Romans, completed about the year 146 B.C., was the most important episode in ushering in the Dark Ages" is rather startling. That Rome had certain military victories over Grecian states is true, but the intellectual conquest remained with the Greeks, and Athens remained the finishing school for Romans who had any pretensions to culture up to the time of Cicero, and indeed for many years afterwards. The Roman victory at Cynoscephalæ and the sack of Corinth caused scarcely a ripple in the elegant and cultivated life of Athens, which had not, in fact, been reduced to a vassal state.

It is difficult, therefore, to see how the year 146 B.C. can be assigned as the one in which the Dark Ages began. The so-called Dark Ages of the older historians were generally said to have commenced in A.D. 476, with the deposition of Romulus Augustulus, which event was considered to make the end of the Roman Empire. From then till the time of the Renaissance Europe was considered to have been in a condition of chaos and mental stagnation. This view was generally accepted till the eighteenth century, but more critical investigations completely refuted this view, and now

no one with any claim to scholarship speaks contemptuously of the "Dark Ages".

The social structure of Europe in the Middle Ages had its shortcomings, but the fact that it endured for a thousand years and withstood the impact of barbarian invasions and was very little affected by them, indicates that it was fundamentally stable. Europe was united during this period by a common official language and by a community of spiritual interests in a way that it has never been united before or since.

Just after the proclamation of the Institutes of Justinian in the middle of the sixth century, there was drawn up a document of scarcely less importance—the Rule of St. Benedict, which served as a model for all monastic institutions. Amongst other things it insisted that the care of the sick should be placed above every other Christian duty. A great hospital was founded at Monte Cassino and others were established all over Europe.

It is quite erroneous to state that "medical science suffered an almost complete eclipse" during the period of the monastic hospitals. The fact is that there was very little medical science to be eclipsed, and that medical treatment was carried on according to the accepted usages of the time. Efforts were even made towards some sort of preventive medicine, and at isolation of infectious cases. It is safe to say that the only organized effort to combat disease and to give to people physical ease from pain as well as the mental comfort of spiritual consolation was made by the monasteries.

Nor did their work stop there. They housed the destitute, fed the hungry, gave lodging to the traveller, and peace and asylum to the scholar.

Then came the Renaissance. This was a good time to be alive if one were a scholar, or an artist, or a scientist living comfortably under the protection of a wealthy patron, but it was not a good time for the ordinary man whose name does not get into history. It was exhilarating to be wittily abusive of the old order, but it was a bad time for the ordinary man to be sick; for as so often happens in times of social change, those who were most anxious to destroy the old order did little to preserve that which was good in it.

The monks of St. Mary of Bethlehem, who founded their hospital in 1247, would have wept had they been able to see it as Bedlam of the eighteenth century.

Dr. Hull, in his desire to revile the Church of the Middle Ages, becomes muddled in his thinking, for he clearly fails to distinguish between spiritual healing and the healing art as carried out with selfless devotion by spiritually minded people.

Yours, etc.,

135 Macquarie Street, Sydney, May 1, 1954.

D. C. TRAINOR.

The Royal College of Obstetricians and Gynaecologists.

VICTORIAN STATE COMMITTEE.

Lecture-Discussions.

A COURSE of lecture-discussions, of symposium type, of special interest to general practitioners, will be given at the Royal College of Obstetricians and Gynæcologists building, 8 Latrobe Street, Melbourne, as follows.

June 9, 1954, 8.15 p.m: "Habitual Abortion", George Simpson, F.R.C.O.G. (chairman), R. M. Alder, M.R.C.O.G., W. R. Griffiths, M.R.C.O.G., J. W. Johnstone, F.R.C.O.G.

June 23, 1954, 8.15 p.m.: "Cæsarean Section", Ella Macknight, M.R.C.O.G. (chairman), W. Morton Lemmon, F.R.C.O.G., James Smibert, M.R.C.O.G., Lance Townsend, F.R.C.O.G.

July 14, 1954, 8.15 p.m.: "Vaginal Discharge", J. G. O'Donoghue, M.R.C.O.G. (chairman), L. W. Gleadell, F.R.C.O.G., A. M. Hill, F.R.C.O.G., D. F. Lawson, M.R.C.O.G.

July 28, 1954, 8.15 p.m.: "Hyperemesis, Cramps, Heartburn, Varicose Veins", W. D. Saltau, F.R.C.O.G. (chairman), B. H. Anderson, M.R.C.O.G., R. M. Rome, M.R.C.O.G., R. G. Worcester, F.R.C.O.G.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MAY 1, 1954.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1(1)	5(4)	1(1)	..	2(1)	..	..	..	9
Amœbiasis	..	..	1	..	..	..	..	..	1
Ancylostomiasis	35	..	..	..	..	..	4	..	39
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1(1)	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(2)	14(13)	3(1)	..	..	..	1	..	22
Diphtheria	11(6)	4(1)	2(2)	..	5(5)	..	..	..	22
Dysentery (Bacillary)	..	2(2)	2(2)	..	..	..	..	..	4
Encephalitis	..	..	..	1(1)	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	8	15(8)	..	..	2(1)	..	..	2	22
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1(1)	4(3)	..	..	..	1(1)	..	..	6
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	17(7)	14(7)	..	4(4)	14(5)	..	..	1	50
Puerperal Fever	1	..	1	..	4(2)	..	..	..	2
Rubella	..	5(3)	..	..	..	..	..	..	9
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	20(11)	36(12)	5(2)	4(2)	1(1)	1(1)	..	..	67
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	2(1)	..	1(1)	..	..	..	4
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	45(35)	21(17)	15(5)	5(5)	8(5)	5	..	..	99
Typhoid Fever	1(1)	..	1	..	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	1(1)	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The fee for the course of four lecture-discussions is £1 11s. 6d., or 10s. 6d. for individual lectures. Supper will be provided after the discussion. Fees may be paid to the Secretary, Royal College of Obstetricians and Gynecologists, 8 Latrobe Street, or on admission to the meeting. As the grounds are not yet completed, it is suggested that the entrance at 9 Victoria Street be used.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Course in Occupational Medicine.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a full-time course in occupational medicine will be held for one week, beginning May 31, under the supervision of Dr. Gordon Smith. Fee for attendance is £3 3s., and enrolments will be received from medical practitioners up till May 28. Written application, enclosing remittance, should be forwarded to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephone: BU 5238, BW 7483; telegraphic address: "Postgrad Sydney."

The programme will include lectures and excursions. The subjects of lectures, which will be held during morning sessions at the School of Public Health and Tropical Medicine, University of Sydney, will include "Radioactivity Hazards" (Dr. C. E. Eddy), "Sickness and Absence Recording" (Dr. C. G. Roberts), "Occupational Mortality" (Dr. H. O. Lancaster), "Accident Prevention and Safety in Industry" (Mr. J. A. Fraser, Mr. J. G. Holdsworth, Mr. W. I. Stewart) and "Tuberculosis in Relation to Occupation" (Dr. Cotter Harvey and Dr. M. P. Susman). Visits will be paid to the Defence Standards Laboratories, the Water Board City Tunnel, the Anti-Tuberculosis Association's Chest Clinic, and the Workers' Compensation Commission.

Notice.

SERVICES MEDICAL OFFICERS ASSOCIATION OF NEW SOUTH WALES.

THE following notice is inserted at the request of the honorary treasurer of the Services Medical Officers Association of New South Wales.

This is to notify all members of the Services Medical Officers Association of New South Wales that on April 23, 1954, the above Association was dissolved in accordance with rule 29 of the constitution, and the assets of the Association, which were £261 17s. 4d., were presented to Sydney Legacy.

CROCKER TESTIMONIAL FUND.

MR. CHARLES CROCKER, who for more than fifty years was associated with the lay staff of the Royal Prince Alfred Hospital, has recently resigned his position. A testimonial fund is being collected as a mark of appreciation of Mr. Crocker's services to the hospital. Any ex-students or ex-resident medical officers of the hospital who care to contribute to this fund are asked to send their donations marked "Crocker Testimonial Fund, R.P.A.H., Camperdown".

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

McKenna, Keith Patrick, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952), 204 Anzac Highway, Plympton, South Australia.

Barker, Shirley Bowman, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953), "Caithness", Mount Barber, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Willing, Richard Lyall, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953); Bampton, John Charles, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953); Cameron, Cyril Thomas Murray, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953); Wheaton, Malcolm Alfred, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953); Swiggs, Francis, M.B., B.S., 1954 (Univ. Adelaide) (qualified 1953).

Deaths.

THE following deaths have been announced:

PITT.—Alan Turner Paul Pitt, on April 30, 1954, at Greenslopes, Queensland.

WILLING.—Charles Eric Willing, on May 1, 1954, at Burwood, Victoria.

WADE.—Robert Blakeway Wade, on May 13, 1954, at Bathurst, New South Wales.

Diary for the Month.

MAY 25.—New South Wales Branch, B.M.A.: Ethics Committee.
MAY 26.—Victorian Branch, B.M.A.: Branch Council Meeting.
MAY 27.—New South Wales Branch, B.M.A.: Branch Meeting.
MAY 27.—South Australian Branch, B.M.A.: Scientific Meeting.
MAY 28.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.
side Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.